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An International Review of Cost-Effectiveness Studies for Mental Disorders

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1. RATIONALE AND BACKGROUND

Mental health services have as their primary and central objective the alleviation of symptoms. However, it is also widely recognised that economic considerations need to be taken into account.

One reason is the widespread recognition that the costs of mental disorders can be substantial, falling on those who are ill, their families, the health care system and the wider national economy. A second reason is the apparently growing cost of treatment. Some of the newer modes of treatment for mental health problems – for example, the newer medications for depression, the atypical antipsychotics for schizophrenia and the cholinesterase inhibitors for Alzheimer's disease – are marketed at higher prices than the older treatments they could potentially replace. This has raised questions as to whether the newer treatments are cost-effective.

But the fundamental and most important reason for being interested in the economics of mental health is because the professional, pharmaceutical and other resources required to treat disorders and to provide support are not enough to meet all needs. Scarcity is a pervasive feature of all health systems, indeed of all societies. In the face of such scarcity, choices have to be made between alternative uses of the same resource or service. Economics – and, in particular, economic evaluation - aims to provide decision makers with data that can inform and assist their decisions as to how to allocate available resources.

The purpose of this report is to look at how economic evaluation methods have been applied in the mental health field. We review the empirical evidence – quite substantial in some clinical areas, and disappointingly sparse in others – from across the world. We structure the review by diagnostic group, looking in turn at:

- child and adolescent mental health problems
- schizophrenia and other psychoses
- depression
- anxiety disorders
- eating disorders; and
- mental health problems in old age.

2. ECONOMIC EVALUATION IN HEALTH CONTEXTS

Decision makers face two central questions when considering whether to use or recommend a particular form of treatment for a specified mental health problem. The first is the clinical question, which asks whether a treatment is effective in improving patient health, or – when considering two or more treatment options – which of them has the better or best outcomes. Once the decision maker knows that the treatment is effective, s/he wants an answer to the second question: is it cost-effective? That is, does the treatment achieve the improved patient outcomes or quality of life at a cost that is worth paying?

These two questions (Is the treatment effective? Is it worth it?) lie at the heart of cost-effectiveness analysis. And while it is always going to be necessary to reformulate these questions in ways that make them answerable with empirical research, their simplicity should never be forgotten. Providing answers to these questions is not so simple.

It must also be emphasised that cost-effectiveness analysis does what its name suggests: it looks at both costs and effectiveness (outcomes). So, comparing the costs of one treatment with another, without any evidence on outcomes, does not constitute an economic evaluation. Such an exercise might be an interesting description of service utilisation patterns and associated costs, conducted with considerable devotion and skill, but it does not provide enough information to assist service professionals, managers or others facing the choice between two or more alternatives. Similarly, calculating the costs and outcomes of a single service could be interesting but cannot be classed as an economic evaluation unless those costs and outcomes are compared with equivalent data for another service, or even compared with the option of 'doing nothing', and so again the study cannot tell us whether the service is worth providing. Uncontrolled mirror design studies often run into this problem.

Before presenting the evidence on cost-effectiveness we therefore need to introduce the modes of economic evaluation and (for each) briefly explain their data needs, advantages, disadvantages and uses (what questions they address). We can also comment on the extent of their use in practice in health economics generally, and in mental health in particular. Subsequent sections will report evidence on the use of these methods, structured by type of mental health problem. Here we will mention one or two mental health examples of each evaluative mode, and those illustrative studies will be discussed in more detail in their respective evidence sections.

Excellent accounts of health economic evaluation methods (although with very few mental health examples) are given by Drummond (1997) and Drummond and McGuire (2001). Byford et al (2003d) offer an introductory account of these methods applied to the social welfare field. The methods of health economic evaluation are, however, developing quite rapidly and some of the techniques mentioned later in this report have been in use in empirical studies for only a short time.

Cost-offset studies

The simplest of economic studies are concerned only with costs, not (usually) because they see outcomes as irrelevant but because, in relation to the treatments or services under study, the health and quality of life outcomes have already been established from other research, or are (currently) not measurable because of conceptual difficulties or research funding limitations. One of these cost-only methods is the cost-offset study, which compares costs incurred with (other) costs saved. For instance, a new drug may have a higher acquisition cost (higher price) compared to an older drug, but may reduce the need for in-patient admissions and thus lead to cost savings downstream. (An example is provided by Hamilton (1999) in the context of a fuller economic evaluation.)

While a cost-offset study is not an economic evaluation, and therefore cannot answer the 'Is it worth it?' question, it nevertheless addresses an issue that is often fundamental to health system decision-making. Within a fixed or even shrinking budget (at least in the short run), are practice changes affordable?

Cost-minimisation analysis

Another 'cost-only' approach is cost-minimisation analysis, which seeks to find which of a number of treatment options has the lowest cost. A cost-minimisation analysis is carried out in one of two ways. It often proceeds in the knowledge that previous research has shown outcomes to be identical in the treatment or policy alternatives being evaluated. One illustration would be the randomised controlled trial of case

management for homeless mentally ill people by Gray et al. (1997) which found lower costs for the case-managed group (although the difference was not statistically significant, raising some important methodological issues). This cost analysis followed some months after the clinical evaluation (Marshall et al. 1995). In this sense the approach is really more accurately described as an 'interrupted' cost-effectiveness analysis (see below). The other way a cost-minimisation analysis can proceed is to compare costs without any regard for outcomes. Such an approach is too narrow and should never be encouraged: it is not an economic evaluation.

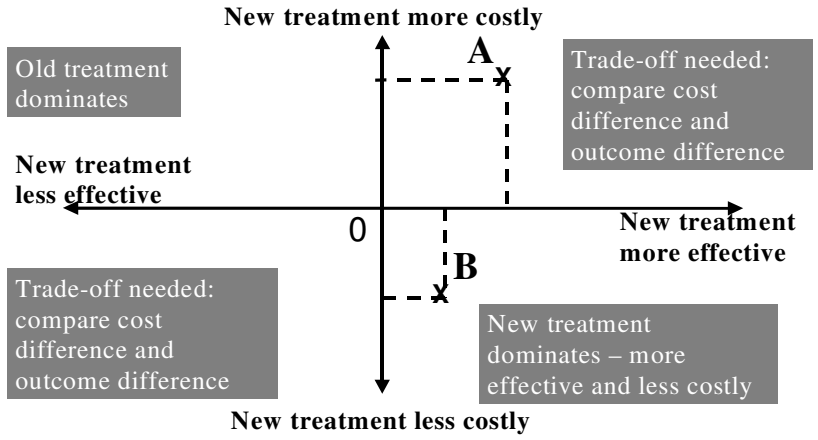
Well-conducted cost-minimisation analysis can be thought of as being a special type of cost-effectiveness analysis, where evidence on effectiveness demonstrates no difference between two or more interventions. In most instances, however, clinical outcomes will not be equivalent, and more complex evaluations are required, which can make them far more informative, but correspondingly more complex to conduct. Nowadays, these other forms of economic evaluation are commonly carried out alongside clinical trials.

Cost-effectiveness analysis

Probably the most intuitive and straightforward modes of economic evaluation are cost-effectiveness and cost-consequences analyses. Both measure outcomes using instruments and scales familiar from clinical studies. Both are employed to help decision makers choose between alternative interventions available to or aimed at specific patient groups. A cost-effectiveness analysis (CEA) looks at a single outcome dimension - such as the number of life years saved, the number of symptom-free days or the duration of time to relapse - and then computes and compares the ratio of the difference in costs between the two treatments being evaluated to the difference in (primary) outcome (the incremental cost-effectiveness ratio or ICER). For example, Essock (1996) computed costs and scores on the Brief Psychiatric Rating Scale for patients given clozapine and those given other medication in three US state hospitals.

A common problem is that the majority of evaluations of new treatments or interventions find them to be both more effective (the outcome profiles are better than for old treatments or interventions) and simultaneously more expensive. Decision makers therefore face the challenge of weighing up the outcomes against the higher expenditure necessary to secure them. The decision is far from straightforward in these cases. The widely used cost-effectiveness 'plane' illustrates the range of possible CEA results and the difficult decision making task.

Figure 1: The cost-effectiveness plane



The cost-effectiveness plane is illustrated in Figure 1, and shows the possible combinations of outcomes and costs when comparing two interventions or treatments. The point marked as B indicates that the new treatment (say a new drug) is both more effective (it has better outcomes) and less costly than the old treatment. In these circumstances the task for the decision maker looks quite straightforward: recommend wider use of the new treatment. However, many of the new interventions being introduced or considered for introduction in health systems are more like point A: they produce better outcomes than older interventions but at a higher cost. The decision now is more complex, because a trade-off is needed: are the better outcomes worth the higher costs?

To aid such decision making, economists have developed cost-utility analysis (see below) and more recently the net benefit approach, linked to the construction of cost-effectiveness acceptability curves (CEACs). These show the probability that a new intervention will be cost-effective for each pre-specified or implicit valuation of an outcome improvement by the decision maker. Comparisons are then possible across quite disparate clinical areas (comparing, for example, schizophrenia treatment with dementia treatment; or psychiatry with oncology). This kind of decision context is, of course, exactly the one faced by decision makers one or two steps removed from the patient interface. An example of the use of the net benefit approach and acceptability curves is provided by Byford et al (2003b), linked to the clinical evaluation reported by Tyrer et al (2003).

An obvious weakness with the strict cost-effectiveness methodology is the enforced focus on a single outcome dimension (in order to compute ratios) when most people with mental health problems have multiple needs for support and when most clinicians would expect to achieve improvements in more than one area. Carrying multiple outcomes forward in an analysis is less tractable analytically, but three options are available, associated with three other modes of economic evaluation. One option - which is cost-consequences analysis - is to retain all or most outcome dimensions (using standard clinical scales). The other two options weight the outcomes, either in terms of money (cost-benefit) or in terms of utility (cost-utility).

Another weakness in the whole approach is that most interventions have never been evaluated properly, so that comparators in trials may not always be appropriate and

the opportunity costs within health care systems of narrow economic evaluation outcomes may be unfavourable (see Oliver et al. 2002, for a discussion of this).

Cost-consequence analysis

A cost-consequences analysis has the ability to evaluate policies and practices in a way that arguably comes quite close to everyday reality. For each treatment alternative the evaluation would compute total (and component) costs and would measure change along every one of the relevant outcome dimensions. The cost and outcome results would need to be reviewed by decision makers, the different outcomes weighed up (informally and subjectively), and compared with costs. For example, the researcher could compute a series of ICERs (one for each measured outcome) for presentation to the decision maker. The decision calculus is therefore certainly much less tidy and more complicated than when using cost-effectiveness ratios or monetary or utility measures of impact (see below), but it could be argued that decision-makers in health care systems - from strategic policy-makers at macro level to individual professionals at micro level - face these kinds of decisions daily.

On the other hand, the weighting of the various outcomes is implicit, subjective and 'technocratic', whereas the choice of the single outcome dimension in a CEA and the weighting algorithms in other evaluative modes are explicit, less susceptible to influence from the value positions of one or two individuals, susceptible too to post hoc rationalisation, and (potentially) reflective of societal values. One example of 'cost-consequences analysis' is a study of motivational interviewing to improve adherence with medication which looked at costs, insight, attitudes to medication, global functioning, symptoms and of course adherence (Healey et al. 1998).

Cost-utility analysis

An increasingly popular evaluative mode that seeks to reduce outcomes to a single dimension is cost-utility analysis (CUA), which measures and then values the impact of an intervention in terms of improvements in preference-weighted, health-related quality of life. The value of the quality of life improvement is measured in units of 'utility', usually expressed by a combined index of the mortality and quality of life effects of an intervention. The best-known and most robust index is the Quality Adjusted Life Year (QALY). CUAs have a number of distinct advantages, including using a unidimensional measure of impact, a generic measure which allows comparisons to be made across diagnostic or clinical groups (for example, comparing psychiatry with oncology or cardiology), and a fully explicit methodology for weighting preferences and valuing health states. But these same features have sometimes been seen as disadvantages: the utility measure may be too reductionist, the generic quality of life indicator may be insufficiently sensitive to the kinds of change expected in schizophrenia treatment, and a transparent approach to scale construction paradoxically opens the approach to criticism from those who question the values thereby obtained (Chisholm et al. 1997).

On the other hand, CUAs avoid the potential ambiguities with multi-dimensional outcomes in cost-consequences studies and are obviously more general than the single-outcome CEA. The transparency of approach is also to be welcomed. The result is an incremental cost-utility ratio for each intervention, relative to some comparator, which can be compared with similar ratios for other interventions (potentially from across the widest diagnostic range i.e. not just from mental health). These cost-per-QALY-gain ratios can then inform health care resource allocation decisions or priority setting.

Cost-benefit analysis

Cost-benefit analysis (CBA) addresses the extent to which a treatment or policy is socially worthwhile in the broadest sense: Do the benefits exceed the costs? This would allow decision makers to consider the merits not only of allocating resources within health care, but also to consider whether it would be more appropriate to invest in other sectors such as housing, education or defence (Tudor-Edwards & Thalany 2001). All costs and benefits are valued in the same (monetary) units. If benefits exceed costs, the evaluation would recommend providing the treatment, and vice versa. With two or more alternatives, the treatment with the greatest net benefit would be deemed the most efficient. CBAs are thus intrinsically attractive, but conducting them is especially problematic because of the difficulties associated with valuing outcomes in monetary terms.

Some CBAs have chosen to focus on a subset of the outcomes. A good example is the classic evaluation of assertive community treatment (ACT) by Weisbrod (1980), which compared a quite wide measure of costs with a relatively narrow monetary outcome: patient earnings from employment. A CBA of this kind can describe only a part of the overall impact of an intervention, in this case the employment effect of ACT, but fortunately Weisbrod and colleagues also used what we would now call a cost-consequences approach, covering a larger set of outcome domains.

Recent methodological advances in health economics offer a way to obtain direct valuations of health outcomes by patients, relatives or the general public. These techniques ask individuals to state the amount they would be prepared to pay (hypothetically) to achieve a given health state or health gain, or observe actual behaviour and impute the implicit values (see Diener et al. 1998). However, they are likely to be quite difficult to apply in mental health contexts. Another approach that has been developed and is increasingly used to value health interventions is 'conjoint analysis'. Individuals are asked to rank different real world scenarios, which may consist of several dimensions (including, for instance, health outcomes, time inputs, discomfort, possible externalities and stigma) and by including cost as one of these dimensions a monetary value can be elicited. While complex, this approach has the advantage of not specifically asking individuals to put a monetary value on health states or health gain, which can make the technique easier to administer than traditional willingness to pay studies (e.g. see Ratcliffe 2000; Ryan 1999). Conjoint analysis has apparently not yet been used in mental health contexts.

3. EVIDENCE: CHILD AND ADOLESCENT MENTAL HEALTH PROBLEMS

The economic dimensions of treatment settings for mental health problems experienced by children and adolescents have been examined in the literature, but not very often. Given the enormity of the morbidity it is very disappointing that so little work has been done in this field. The studies that have been completed have looked at the roles of hospital and community based models of service delivery, medications, psychological treatment, approaches involving skills development, educational programmes, support system interventions and care management approaches. A review of published economic evaluations in this field a few years ago revealed a narrow evidence base of interventions for mental health problems in childhood and adolescence (Knapp 1997a). More recently we conducted a systematic review that identified fourteen studies assessing both costs and outcomes (Romeo et al. 2004a).

They covered a range of treatments for mental health problems specific to children and adolescents.

The economic evidence in this area will cover pharmacotherapy, psychological interventions and social and community context of treatment (the latter covering approaches involving educational and skills interventions, early intervention services and comprehensive and coordinated service approaches).

3.1 Pharmacological interventions

Since the 1950s stimulant medications such as methylphenidate and amphetamines have been used as therapy for hyperactivity and impulsive disorder in children. A review of the literature on the effectiveness of methylphenidate shows that the short-term treatment of hyperkinetic children with methylphenidate is effective. However, the medium to long-term effects is still in the balance. Methylphenidate is the only pharmacotherapy for hyperactivity identified in the review that has undergone an economic evaluation to date. Gilmore and Milne (2001) created an economic model that compared the costs and effects of methylphenidate and placebo. Costs were calculated based on the assumption that all follow-ups would be hospital-based. Non-responders and those terminating treatment would be treated on average for 6 weeks. There would be an average of five outpatient attendances in the first year of treatment, followed by three-monthly routine appointments. The authors have acknowledged the methodological limitations of the framework used in the study. However, they conclude that the short-term treatment of hyperkinetic children with methylphenidate may be cost-effective.

Traditional mood stabilizers such as lithium, neuroleptic therapy, valporate, carbamazepine, and chloropromazine are the mainstay of treatment in adolescent bipolar disorder. However, data from open trials suggest that under certain conditions lithium and valproate may be effective in controlling mood symptomatology, whereas valproate may be better tolerated in adolescents. Further research of children whose acute manic episode is unresponsive to pharmacotherapy has described successful electroconvulsive treatment (ECT) (Betagnolli & Borchardt 1990; Carr et al. 1983; Warnecke 1975). Kutcher and Robertson (1995) studied the cost-effectiveness of ECT compared with standard pharmacological treatment for bipolar disorder. ECT outcome was significantly better than for the pharmacological group. Mean cost per hospitalisation was less than half that of the non-ECT treated group. The authors are cautious in their conclusions, stating that ECT may be cost-effective in comparison to standard psychopharmacological interventions. The limitations of this study make it impossible to conclude otherwise given the use of chart review and the further limitation of the small sample of children in each group.

3.2 Psychological interventions

A range of delivery formats for psychotherapeutic intervention exists and may involve the individual child, group, or family. Despite the many and varied treatments, only a few economic evaluations have been investigated. The body of evidence has focused on behavioural therapy for the treatment of behavioural disorders and other externalising behaviours. More specifically parent management training is one of the most extensively studied behavioural therapies for children and reviews of the literature have shown it to be effective in decreasing oppositional, aggressive, and antisocial behaviour (Dumas 1989; Forehand & Long 1988; Kazdin 1985; Miller & Prinz 1990).

Thompson and colleagues (1996) investigated the cost-effectiveness of parents of children with behavioural disorders being assigned to parent training or a waiting list. The findings indicate that parents who completed the parent-training programme reported an improvement in their child's externalising behaviour, improvement in parent's self esteem and sense of competence and an increased overall satisfaction with family relationships. These results were compared with the direct cost of treatment, but the authors rightly state that the results are limited. One reason is that the non-random allocation to the treatment groups may have resulted in the observed differences being due to a placebo effect since the control group did not receive any treatment.

Prior research on children with behavioural problems conducted by Christensen and colleagues (1980) sought to evaluate the efficiency in the delivery of treatment formats. The study evaluated 36 families divided into 12 blocks of three families and randomly assigned to group training, individual treatment and minimal contact bibliotherapy (MCB). Evidence of effectiveness was based on three treatment measures of parent attitude, parent observation data and home observation collected at treatment termination. Costs were measured in terms of the average professional time expended per family. MCB participants spent only 49 minutes, on average, with the professionals, as compared to over five hours for group sessions and over 11 hours for those receiving individual treatment. MCB performed as well as the other groups in terms of parent attitude towards the child. Based on this criterion, MCB would be the treatment of choice. However, the findings also indicate that there were significantly larger reductions in problem behaviours under clinical conditions than for the MCB intervention, with no significant difference between group and individual treatment therapies. With a more robust view of treatment outcome based on both the parent attitude and the child's behaviour, both the group and individual conditions are more effective than MCB. However, group therapy requires half as much professional time as individual therapy.

Routine psychological interventions for behavioural disorders such as parent training can be delivered in a variety of settings. However, while little is known about the relative cost-effectiveness of behavioural interventions for antisocial behaviour in children, even less is known about which delivery location of treatment offers comparative value for money. Cunningham (1995) sought to assess the cost-effectiveness of a large group community-based training programme compared to a clinic-based individual intervention. Outcome measures included adherence, behaviour problems at home, problem solving skills, parenting sense of competence and parent child interactions. Cost measures were based solely on programme cost. Community groups reported enhanced utilisation, greater reduction in child management problems and better maintenance of gains at follow-up, which contrast to the findings of other studies which report outcomes of small group parent training comparable to individual intervention. Lower costs were incurred in the community groups compared to those receiving individual training. This finding contrasts with that of Harrington and colleagues (2000) who found no significant differences between community and hospital-based groups on any outcome measure or on costs. More decisively the authors conclude that the location of treatment is less important than the range of services provided.

3.3 Social and community context of treatment

Early economic evidence on the relative merits of hospital and community-based services was provided by Kiser and colleagues (1987) looked mainly at costs of

children presenting a wide variety of disorders. The authors found no significant cost difference between hospital and day care.

In a later paper Grizenko & Papineau (1992) evaluated the cost-effectiveness of day treatment and residential care for children with severe behavioural problems, using retrospective chart reviews. Costs were based on yearly operating costs and included monies paid out to all professionals. Total operating cost data were combined with total possible days of attendance (total yearly cost/total possible days of attendance) to derive the daily cost of treatment. Daily costs before 1989 were indexed to yield costs in constant 1989-90 dollars. The findings of the study indicate that each treatment group showed a significant improvement in the level of school integration and the level of clinical improvement. The range of daily costs for day treatment was less than for inpatient treatment. Total costs for the day treatment group were significantly less than for the residential group. Though there are limitations with the design, the findings pave the way for further prospective research in this area.

Byford and colleagues (1999) evaluated the costs and effects of routine care plus a home-based social work intervention in comparison to routine care alone for deliberate self-poisoning in children and adolescents (age 16 or under). Outcomes, assessed at baseline, two and six months included suicidal ideation, feelings of hopelessness and family functioning. Costs included all health, education, and social services. No statistically significant differences were found between the two groups in terms of any of the outcome measures. In a sub-group of children with major depression, suicidal ideation was significantly lower in the intervention group, with no significant difference in cost. The authors reject the hypothesis that the experimental intervention is more cost-effective than routine care overall but suggest that it may be more cost-effective for this sub-group of children. They argue that further research is needed.

Education and skills development interventions

A variety of novel techniques has been found to be effective in treating mental illness in children. Clinicians have suggested the use of non-pharmacological therapies such as individual therapy, social milieu therapy, family therapy, and psychoeducational therapy for children diagnosed with schizophrenia. Nevertheless, it is not clear whether psychoeducational treatment has any effects on young people with very early-onset schizophrenia. Rund et al (1994) evaluated the effectiveness and costs of a psychoeducational intervention compared to standard care for the treatment of adolescents (age 13-18) with early onset schizophrenia. Outcomes assessed over the two-year treatment period included psychosocial functioning and relapse rates. The cost perspective was relatively broad, including inpatient treatment, home visits, consultations with a private medical doctor or clinical psychologist, social welfare services and the cost of seminars for parents, including travel and other expenses. The authors conclude that the more effective intervention, the psychoeducational programme, was also the cheapest. In common with many other studies in this review, this evaluation suffers from a small sample size and a retrospective design, at least for the control group. The sample is too small to have any confidence in the statistical tests and bias between the two groups is a possibility, although the process of matching the controls will have helped to limit systematic differences.

Treatment programmes that teach social competence skills often incorporate social skills training, another form of psychological treatment. Two economic evaluations have been conducted to date using this approach, both targeted at children with antisocial behaviour. In the first paper Slot and colleagues (1992) report their cost and

outcome comparison between the teaching family model and a traditional state institute for antisocial behaviour in young people. Comparison of effectiveness was made on three dimensions: problems, ability to form relationships outside the family, and abilities for community participation. On the first and second outcomes there were no differences between the two interventions. On the third dimension young people in the state institute showed improvement whereas young people in the teaching family model did not change. Further analysis showed that the teaching family model sample improved on two measures within the third dimension (number of months in employment or enrolled at school, and academic and vocational aspirations), but these improvements were outweighed by an increase in alcohol consumption. The teaching family model was much less costly than treatment in the state institute. This very simple study did not measure costs very broadly (although the authors note that there were no differences in the use of after-care services), the sample was small, matching was quite limited, and analyses were also very limited (there was no testing for significance).

In a second paper, Jones and Offord (1989) compare two publicly supported housing schemes. The intervention was coined the PALS ('participate and learn skills') programme and was aimed at skill development. It employed two full-time staff (for approximately 417 children, although numbers fluctuated as they were defined by the housing scheme population). All children in the housing scheme were informed of the activities and participation records were kept. Non-participating children were especially encouraged. The control site, another housing scheme, had 'a lower-key, recreation-and-activity programme aimed mainly at participation'.

Outcomes were better for the PALS site than for the comparison housing scheme in terms of skill development and integration (not tested for significance), as well as self-esteem, security violations and fire calls. Costs were only measured for the PALS programme (all personnel and other costs) on the assumption that this represented the differential cost between sites. These costs were compared with savings resulting from the observed decreases in charges against juveniles, number of security reports and number of fire calls. Only immediate and not longer-term savings were examined. Savings were estimated to be substantially greater than the PALS programme costs.

The PALS study has a number of limitations as an economic evaluation. Allocation to groups was not by randomisation, but comparisons between experimental and control sites were not adjusted for characteristics of the children. Costs are of course only measured for the add-on programme and it is therefore not possible to examine whether there were changes in other service utilisation. Opportunity costs appear not to have been calculated. No adjustments were made for differential timing. The innovative cost-offset comparison (called a 'cost-benefit analysis' by the authors although we would hesitate to use this label ourselves, even though there is no unambiguous division between costs and outcomes, for savings that result from reduced service use are likely to result from reduced individual needs, and the latter can be called outcome) is based on conservative costings for criminal justice, fire department, and housing damage costs. Although the analyses have some limitations it is unlikely that these alter the conclusion that savings outweigh the costs of the programme.

Early intervention services

Early detection and treatment may be one method of counterbalancing future costs to service providers and effects to beneficiaries of these services. The only study uncovered by our review that looks at the costs and effectiveness of early intervention

services is a study by Mihalopoulos et al (1999). The authors evaluated a phase-specific community-orientated treatment of early onset psychosis (EPPIC) versus standard care. The EPPIC intervention consisted of an early psychosis assessment team, inpatient unit, outpatient case management, day programme and smaller therapeutic programmes. The design was a before-and-after study comparing 51 EPPIC patients treated between 1993 and 1994 with 51 matched retrospective controls that received the pre-EPPIC treatment model between 1989 and 1992. Outcomes assessed included quality of life and negative symptoms. The cost perspective was limited to health services and included the cost of inpatient stays, outpatient appointments, medication, community mental health team (CMHT) contacts, general practitioner contacts and private therapy and psychiatry.

EPPIC was found to cost less than the pre-EPPIC treatment model, although there is no indication of the statistical significance of this result. The difference in cost was the result of reductions in inpatient costs that outweighed increases in community services. Outcomes were reported in a previous publication and not repeated except that EPPIC achieved better outcomes, again with no indication of statistical significance. The authors calculate the average cost per unit improvement in both the SANS and the QLS, but fail to undertake an incremental analysis. The authors conclude that EPPIC was a more cost-effective intervention than the pre-EPPIC treatment model, but suggest that these results are not conclusive and further research is required. One of the main limitations was the use of retrospective controls and the lack of randomisation, although the use of matching may have reduced some of the bias that results from such designs. The authors also point out some of the costing limitations of the study, such as the exclusion of the cost of the pre-treatment phase, capital and other hidden costs, which they suggest would increase the cost of the EPPIC group. However, the use of sensitivity analyses, to test such exclusions found the results to be robust. The small sample sizes involved are an additional weakness.

Coordinated or comprehensive services

Two studies have evaluated the cost-effectiveness of multiple interventions for mentally ill children and adolescents. Erickson-Warfield (1995) reports on an analysis of costs and cost-effectiveness of alternative forms of early intervention services in Massachusetts. The sample of 157 children included children with Down's syndrome, motor impairment and developmental delays of uncertain aetiology. Data were collected on the type, amount and estimated value of all services received by each sample member. Outcomes were measured to assess different aspects of social competence: adaptive behaviour (communication, daily living skills, socialisation, motor skills) and the child's ability to interact with their mother.

For each of six service types - home visits, group services, centre-based individual, parent support group, screening, assessment - multiple regression analyses examined changes in adaptive behaviour, child-mother interaction, mother-child interaction and parenting stress as a function of pre-intervention scores, hours of service received for each of the six service types, disability, age, Down's syndrome and family income. These are effectively cost and production function estimates. The results suggest that the service identified as more cost-effective varied by sub-group (child disability and age etc) and outcome measure. Among other things these analyses suggest that group services are more efficient than home visits. However, it is difficult to generalise because of the quite large number of different analyses undertaken.

In a second evaluation conducted more recently, King and colleagues (2000) compared a continuum of care approach with traditional mental health services. The

former consisted of the Fort Bragg Demonstration project, involving a continuum of care services, and two comparison sites that provided traditional fee-for-service mental health services. This prospective, quasi-experimental study included 59 adolescents with co-morbid substance use. Outcomes were assessed at baseline and six months later and included substance use, impairment level specifically attributed to substance abuse, mental and physical impairment, caregiver strain and global functioning. Costs included all mental health services provided.

The study served a number of different purposes, in addition to the assessment of costs and outcomes. The authors do not come to any specific conclusion regarding relative cost-effectiveness, although it appears that the demonstration site may be less cost-effective than the control sites. Any conclusion, however, must be viewed cautiously given the small sample sizes involved and the possibility of bias due to the lack of randomisation or adjustment for differences between the two groups.

3.4 Conclusions

When the studies examining the cost-effectiveness of interventions in child and adolescent mental health are taken together, they reflect the potential for devising innovative, targeted problem-specific treatments and coordinated services. Regrettably, economic research in this area is not at all plentiful and is patchy in quality. Inconclusive findings often arise due to small sample sizes, methodological weaknesses and other design issues. As a consequence, for example, the cost-effectiveness of pharmacological interventions for children and adolescents with mental health problems is doubtful. A broader evidence base for cost-effectiveness exists for behavioural disorders using psychological interventions, though many studies here suffer from design limitations. Overall, the findings suggest that the range of services provided is more important than the location of treatment. However, the cost-effectiveness of other novel approaches including new educational interventions, social skills interventions and comprehensive services across diagnostic groups is less well established. To date the strongest evidence for cost-effectiveness in the child and adolescent mental health area has come from a controlled study of treatment approaches for deliberate self-poisoning in children. Even here, the authors can only tentatively suggest that home-based social work intervention may be more cost-effective than routine care alone for this sub-group of children.

While we are still a long way off finding conclusive answers to many (indeed most) questions about the cost-effectiveness of treatments for children and adolescents with mental health problems, there are a number of developments taking place. Statistical techniques are emerging and discussions surrounding these are taking place in an effort to address methodological issues associated with the design of economic evaluation studies in mental health. We are also aware of a clutch of further studies now underway, including one of the cost-effectiveness of individual versus group psychotherapy for sexually abused girls, recently been completed, one on cognitive behavioural therapy and antidepressants for young people with depression and one on hospital services for young people with anorexia nervosa. Nevertheless, as noted at the beginning of this section, both the volume and quality of the economic evaluation evidence in this area are a long way short of what decision makers need to inform their clinical and strategic decisions.

4. EVIDENCE: SCHIZOPHRENIA AND OTHER PSYCHOSES

The body of economic evidence on treatments for schizophrenia has grown to quite a reasonable size, and there are some good quality studies that are already proving

helpful to health system decision makers. Evaluations of treatments for other psychoses are much less common. In this section we review this evidence in some detail, looking first at pharmacotherapy and psychosocial treatments, and then turning to evidence on community-based treatments for working age adults with mental health problems. The reason for including this last set of studies here is because people with schizophrenia or other psychoses have dominated the samples in most of the completed studies of community care arrangements. The fourth subsection looks at treatments for people with bipolar disorder.

4.1 Pharmacological interventions

Side-effects and non-concordance

Pharmacotherapy is the first-line treatment for patients presenting with acute psychotic symptoms. It reduces both the incidence of positive symptoms and the risk of subsequent relapse. However, a problem with conventional neuroleptics is that many patients do not want to take them, and non-concordance (or non-adherence) can push up costs. Many factors are associated with non-adherence, including symptomatology, culture and ethnic group, low response to treatment, a poor patient-doctor relationship and limited insight. Depot neuroleptics have been used in the past to improve adherence but are associated with extra-pyramidal symptoms (EPS) and other side-effects (Sartorius et al, 2002).

The atypical antipsychotics are different from traditional therapies in their effects on positive symptoms and they appear to be associated with lower levels of EPS. Unlike the conventional antipsychotics, some of the atypicals may also reduce negative and depressive symptoms and perhaps improved cognition.

These newer drugs have been called ‘atypical’ because of their chemical action but - colloquially - they might also be seen as ‘atypical’ because of their high acquisition costs (high prices). These higher prices are a bone of contention in some health care systems. Pharmacy managers and some other budget holders have been reluctant to sanction the prescribing of the atypicals, and some national governments have declined to include them on the lists of drugs eligible for partial or full patient reimbursement. There might be unintended consequences. In an earlier period, cost-saving measures by Medicaid in one US state that limited schizophrenia patients to three prescriptions per month (saving $5 per patient) led to patients using more mental health services at an increased cost of roughly 17 times the amount saved on drugs (Soumerai et al. 1994).

Improved tolerability of the new drugs is expected to improve adherence and reduce relapse rates. In turn, this should reduce costs. One of the most pressing questions, therefore, is whether the atypical antipsychotics are cost-effective.

Depot treatments

Despite the continued widespread use of depot antipsychotics in the treatment of schizophrenia in some countries, the quantity and the quality of the available cost-effectiveness evidence for them are limited. Systematic reviews of clinical evidence suggest that, although depot administration has advantages over oral administration for patients who are not well engaged with services or do not regularly take their oral medication, the international evidence on effectiveness is mixed (Adams et al. 2001; David & Adams 2001). Although it has been argued that depot medication is cost saving compared to oral conventional antipsychotics under certain assumptions

(Glazer & Ereshefsky 1996; Hale & Wood 1996), the cost-effectiveness evidence is too poor to draw firm conclusions (Knapp et al. 2002; National Collaborating Centre for Mental Health 2002). However, the non-adherence problem which has often in the past led to the prescription of a depot medication generates quite complex challenges for evaluative research in this area: patients who do not take their oral medication may also be hard to recruit into, or keep in trials or to keep until the end of the study.

Clozapine

The first of the atypical antipsychotics was clozapine, which has now been the subject of many clinical evaluations. The early evaluations of clozapine did not include an economic dimension. One of the earliest demonstrated the superior efficacy of clozapine over chlorpromazine in treatment-resistant schizophrenia in a 6-week, double-blind, randomised controlled trial involving a total of 319 severely ill schizophrenic patients who had failed to respond to at least three standard medications (Kane et al. 1988). At the end of the study, 30% of clozapine patients versus 4% of chlorpromazine patients had clinically significant improvements. A Cochrane Collaboration systematic review of clinical effectiveness has concluded, 'clozapine reduces relapse and symptoms and produces clinically meaningful improvement in patients with schizophrenia' (Wahlbeck et al. 1998).

Most published studies of clozapine cost and cost effectiveness are naturalistic, retrospective, non-experimental analyses or decision models (Morris et al. 1998), although long-term prospective randomised trial evidence has now emerged. Here we focus on the most important studies since recently published reviews address this topic in some detail (NICE 2002; Taylor 2002).

The first economic evaluation was an open, non-randomised study conduced by Revicki (1990). In the clozapine group 65% of patients responded to the therapy and 35% discontinued therapy after a mean period of 80 days (14% for non compliance, 15% for lack of response, 6% for adverse events). After one year of treatment the clozapine group had improved (significant reduction in BPRS) and the inter-group difference had narrowed. Total mean medical costs in the pre-treatment year were about $10000 higher per patient in the clozapine group than in comparator group, although pre-treatment hospital costs for the two groups were similar. Clozapine patients had lower hospital costs during the two post-treatment years. However, the costs for non-hospital services for this group, excluding drug therapy, increased during the first post-treatment year. The clozapine group averaged $10040 more in total costs than the comparator group in the first year after start of treatment, but costs were lower during the second year. Various criticisms have been levelled at this study, relating to the failure to follow-up dropouts (35% of the original clozapine group), the narrow measurement of costs, the inability to match patients at baseline (the clozapine group were more severely ill) and the different measurement approaches employed for the two groups (Frank 1991; Goldman 1991). Nevertheless, after some re-analysis of the data, Revicki (1990) concluded that clozapine produced net cost savings.

There have been numerous similar studies in the USA and in other countries since Revicki's influential study, some focussed exclusively on treatment-resistant patients. Most used modelling, mirror-design or other retrospective evaluations to conclude that clozapine improves symptoms (usually measured on the BPRS and/or CGI) and quality of life, and reduces either hospitalisation or total costs compared to the pre-treatment period. All reach similar conclusions: clozapine improves symptoms and reduces costs.

Two prospective randomised trials in the USA have examined the comparative effectiveness of clozapine and conventional neuroleptics. Economic evaluations were conducted alongside these trials. Essock and colleagues (1996) conducted a randomised open-label study of clozapine therapy versus usual care among patients in three large Connecticut state hospitals (n = 227 patients). The study continued for two years on an intention-to-treat basis (there were a number of crossovers) and found no differences between the groups in relation to symptoms or functioning. However, clozapine had a comparative advantage with respect to avoidance of hospital re-admissions, total time in community settings, EPS side effects and disruptiveness. Compared to the usual care group, the clozapine sample had $1112 higher costs in the first year after randomisation but $7149 lower costs in the second year. These differences (or their sum) did not reach statistical significance. Consequently, clozapine was found to produce better outcomes at a cost that was no different, and was therefore more cost-effective than a range of conventional antipsychotic medication for long-stay patients in state hospitals (Essock et al. 2000).

The other North American RCT compared clozapine and haloperidol treatments for refractory patients who had been hospitalised for 30-364 days in the previous year. The study was based in fifteen Veteran Administration (VA) medical centres across the USA. The results were reported in a series of papers by Rosenheck (1997; 1998; 1999). The clozapine group had better concordance, lower symptom levels (as measured by the PANSS) and improved quality of life (among those who did not cross over to the other treatment, but not in the intention-to-treat analysis). The clozapine group had fewer days of hospitalisation for psychiatric reasons, but used more outpatient services, and had fewer problems with tardive dyskinesia and akathisia. Health care costs were included (inpatient, outpatient and drug therapy) and unusually the study also included many non-health care costs (accommodation, lost productivity, criminal justice, family burden and administration of transfer payments). Costs were higher in the clozapine group for antipsychotic drugs and outpatient care, but these higher costs were more than offset by reductions in hospitalisation costs. Overall, the costs for the clozapine group were $2734 per patient year lower than for the haloperidol group over a 1-year study period (Rosenheck et al. 1997).

In a second paper a cost-utility analysis was carried out based on the Composite Health Index for Schizophrenia (CHIS) and confirmed the results obtained in the cost-effectiveness study (Rosenheck et al. 1998). A further analysis split the sample into ‘high hospital users’ and ‘low hospital users’ (Rosenheck et al. 1999). Clozapine use for the low hospital users did not produce cost savings (mean annual saving of $759 by ITT analysis and -$4140 after excluding crossovers), although there was a significant difference in QALYs gained (2-3%). For the high hospital users there was a large cost saving ($7134 and $4806, respectively), and QALY improvements were greater than for the low hospital users (3.7-4.7%). The authors concluded that clozapine is more cost-effective than treatment with haloperidol for patients suffering from refractory schizophrenia, and especially for patients with high prior levels of hospital use.

Risperidone

A systematic review of the effectiveness of risperidone concluded that this atypical antipsychotic ‘produces greater clinical improvement than conventional neuroleptic agents in patients with schizophrenia and is associated with fewer extrapyramidal side effects’ (Kennedy et al. 1997; Soares 1998). There are no prospective randomised trials which examine the cost-effectiveness of this atypical antipsychotic, but mirror-design and observational studies point to cost-offset advantages.

Retrospective analysis of an open-label clinical trial of risperidone in Canada found that the number of days spent in hospital was reduced by 20% following treatment for those who responded to risperidone, although 64% of patients were non-responders. The resultant sample size was small (n = 27), the economic analysis confined to inpatient days, and the conclusions only preliminary (Addington et al. 1993). An unusual retrospective cost-utility evaluation of a sub-population of patients from this trial revealed that risperidone provided more than double the number of QALYs compared with haloperidol. However, the analysis was so complex that it is difficult to evaluate the robustness of the findings (Chouinard & Albright 1997). Most economic studies of risperidone have employed similar mirror-designs and reached the same conclusion that inpatient days fall, even after making allowance for the general downward trend in psychiatric hospitalisations.

All of these studies suggest that risperidone is likely to be a cost-effective alternative to conventional neuroleptics, but they are open to the same reservations as other uncontrolled mirror-design studies, including being susceptible to sample selection artefacts and historical bias (Taylor 2002). Costs in some studies were quite narrowly measured and outcomes were sometimes not included in the analyses, although of course there are powerful effectiveness results from published randomised trials (Csernansky et al. 2002). Risperidone may not be more cost-effective than conventional neuroleptic treatment outside Western Europe and North America. Hosak and Bahbough (2002) found no cost-effectiveness difference between risperidone and haloperidol in their Czech Republic study. This result - which is at variance with other risperidone studies – probably stems from the low cost of staff resources in the Czech Republic relative to (say) the US, and the relatively high cost of medications. Reductions in the use of in-patient beds would not therefore lead to such marked cost savings to set against the higher expenditure on medication.

Olanzapine

Olanzapine first became available on prescription for treating schizophrenia in 1996. In the absence of long-term economic data alongside clinical trials, Lilly Industries commissioned the development of a decision model to compare the cost-effectiveness of alternative therapies, which was populated by data for each of a number of countries (e.g. Palmer et al, 1998). The five-year model evaluates the expected direct costs of treatment for patients with schizophrenia. Looking across these models, the higher acquisition costs of olanzapine (and risperidone in the US model) compared to haloperidol, are largely offset by a reduction in (assumed) service utilisation associated with better health outcomes - mainly because olanzapine reduces negative and positive symptoms, and also lowers relapse rates. Over one year, the comparison of costs looks to be at least cost-neutral.

An independent study in the UK has modelled the cost consequences of prescribing olanzapine as first and second line treatment (Cummins et al, 1998). A simple model estimated the costs of schizophrenia according to disease severity by estimating resource use by the different groups of people distinguished previously by Davies and Drummond (1994): those with a single episode (average duration 22 weeks); episodes of major disorder lasting up to 1 year; episodes for 1 to 2.5 years; and episodes lasting for more than 2.5 years, stratified by whether receiving community care or hospital care. Resource use was restricted to inpatient and outpatient services, day care and community support. The results projected cost savings associated with olanzapine use compared with haloperidol.

Quite strong economic evidence comes from a 17-country RCT comparing olanzapine (n = 1336) and haloperidol (n = 660) over a 6-week treatment period. Half the sample continued into a responder extension for another 46 weeks. The clinical evaluation found superior outcomes for olanzapine over haloperidol in relation to negative symptoms, EPS profile, prolactin levels and response rate (Tollefson et al. 1997). The economic evaluation, which is reported by Hamilton et al (1999) and focussed on the US sub-sample, found monthly medication costs to be $209 higher for olanzapine than haloperidol in both the acute and maintenance phases, but outpatient and inpatient costs were lower in both phases. Total monthly medical costs in the acute phase were $431 lower with olanzapine (p = 0.026) and $345 lower in the maintenance phase (p = 0.160). No other costs were included in the evaluation. Analysis of the French sub-sample reached a similar conclusion of cost-effectiveness (Le Pen et al. 1999).

However, a different finding is reported by Rosenheck (2003) from a US study, again based on an RCT design. They report no differences between olanzapine and haloperidol in terms of study retention (compliance), positive or negative symptoms, quality of life or EPS; superior outcomes for olanzapine in terms of akathisia, tardive dyskinesia, memory and motor function; and inferior outcomes for olanzapine in terms of weight gain. Costs for the health care provider were also significantly higher for the olanzapine patients.

Other atypicals

A number of other atypical antipsychotics have been licensed for the treatment of schizophrenia. Few economic evaluations have been published (Ereshefsky et al. 1997; Souêtre et al. 1992), and no review is possible at this stage.

Comparisons of different atypical antipsychotics

There are few direct comparisons between the different atypical medications, and most are methodologically weak, often collecting data retrospectively, and sometimes employing rather narrow measures of cost. Their findings do not point consistently in any one direction. Most of these studies have compared olanzapine and risperidone, some pointing to relative hospitalisation and cost advantages for risperidone (Kasper et al. 2001; Kelly et al. 2001; Rabinowitz et al. 2000), and others pointing to relative advantages for olanzapine (Russo et al. 2002; Zhao 2002). In another naturalistic study, Lewis (2001) found no significant cost differences between risperidone, olanzapine and clozapine treatment. The one cost-effectiveness study based on a randomised controlled trial design analysed data for 150 US patients included in a multi-country randomised controlled trial; Edgell (2000) concluded that medication and in-patient costs were lower for olanzapine compared to risperidone patients, but total costs were not significantly different. Superior outcomes led them to conclude that olanzapine was the more cost-effective treatment for this patient group.

4.2 Psychological interventions

An increasingly studied area of schizophrenia therapy covers psychological treatments. There are many psychological and psychosocial approaches to the management of schizophrenia (Tarrier 1996; Wykes et al. 1998), but few have been studied by economists. However, because most psychological treatments, even group sessions, are labour-intensive and sometimes continue for long periods, they may look expensive. An important question to be addressed, therefore, is whether they have counter-balancing outcomes or whether they reduce longer-term costs. A recent global

systematic review found evidence of no effectiveness in the case of several widely applied psychological interventions (National Collaborating Centre for Mental Health 2002). Two areas that have been studied also from an economic viewpoint are concentrated on improving patient adherence with medication treatment and improving family support in community settings.

Improving adherence

We noted earlier that relapse is one of the principal cost drivers or concerns in schizophrenia, and can have high cost implications, especially if a patient needs readmission to hospital. More than one third of the costs of schizophrenia relapse can be attributed to non-adherence with treatment (Weiden & Olfson 1995). Not surprisingly, therefore, care professionals are keen to improve adherence with recommended drug treatment regimes, both to improve the health and quality of life of schizophrenia sufferers in the short term and to reduce the probability of relapse in the longer term. Psychological therapies have an important role to play.

Many approaches have been tried to improve concordance or adherence (Knapp et al. 2003; MacPhillips & Sensky 1998). Education about the nature of the disease and its management has been found to achieve, among other things, significant improvements in taking medications compared with control groups. However, there appears to be no published economic evaluation of a formal psychoeducation programme (National Collaborating Centre for Mental Health 2002). Boczkowski (1985) found that adherence with antipsychotic medication could be improved by measures that built the treatment into patients' everyday activities, and other studies have found similar effects (Kuipers 1996).

A recently published study shows that a short intervention based on cognitive behaviour therapy, called compliance therapy by the clinicians who devised it, can achieve better outcomes at the same cost as standard counselling. Patients were invited to discuss first their attitude towards their illness, and subsequently the drawbacks and advantages of drug treatment. A randomised controlled trial of 74 people with psychosis about to move from inpatient residence found that patients counselled in this way were five times more likely than a control group to take their medication without prompting, and over an 18-month follow-up period had better global functioning, insight, adherence and attitudes to their medication (Kemp et al. 1998).

The economic analysis covered all health and social care services, education, social security and housing supports, and criminal justice contacts, but excluded caregiver and lost employment costs. The cost-consequences analysis found costs to be the same for compliance therapy as for standard counselling during each of the three 6-month follow-up phases and over the full 18 months. Costs were higher for patients with greater symptomatology. Significant correlations were found between greater adherence and higher costs over the first six months. That is, improving adherence will initially increase costs, although over time there is an offsetting reduction (Healey et al. 1998).

Another UK study reported the cost-effectiveness of cognitive behaviour therapy (more broadly focussed) when compared to standard care (Kuipers et al. 1997; 1998). The cost-consequence analysis was based on a randomised controlled trial of 54 patients with schizophrenia spectrum disorders, and covered all health care, community care and accommodation costs. Cognitive behaviour therapy was found to be more effective (in relation to BPRS, delusional distress) and perhaps less costly

than standard care, although the small sample made it difficult to reach firm conclusions on the cost difference.

Both of these studies, evaluating treatments based on cognitive behavioural approaches, thus concluded that this therapeutic mode is not costly in relative terms and that it appears to be efficient when looking at its outcome and resource implications.

Family intervention

A wide range of responses can be expected from families in the care-giving role. Brown et al (1962) described how patients discharged from hospital to their families were more likely to be readmitted than those discharged to live alone or with private landlords. This stimulated interest in the role of the family in the course of schizophrenia and led to the work on expressed emotion (EE) (Vaughn & Leff 1976). Stress, hostility and emotional over-involvement may result in a family with a high level of EE, which may cause further deterioration in the situation, as patients living in high-EE households have a worse prognosis than those in low-EE households.

Family interventions aim to reduce the impact of family stress and conflict often seen in high-EE households (Vaughn & Leff 1976). A systematic review of randomised trial findings whittled down the international literature to 18 studies, employing quite tight selection criteria, particularly in relation to methodology and design, to make the selection. The reviewers concluded that family interventions reduce relapse and readmission rates, improve concordance with medication and decrease carer burden (Leff 1996).

Family interventions may also reduce costs. The most recent economic review of which we are aware identified nine economic studies from the USA, the UK, Germany and China (National Collaborating Centre for Mental Health 2002). Generally, they were not as comprehensive in their coverage of direct and indirect costs as would now be expected, but they complemented the clinical evidence well. Falloon (1982) conducted their randomised trial in Los Angeles, comparing a psychoeducational family programme combined with maintenance drug treatment against drug treatment alone. The relapse rate was substantially lower in the family therapy group – a result that has been replicated in other studies – and there were greater improvements in household tasks, work or study activities and social relations. Caregiver burden was also reduced over both the initial nine months and the full two years of the follow-up period. Three economic studies based their analyses on these trial data (Cardin et al. 1986; Goldstein 1996; Liberman et al. 1987). A (limited) cost-benefit analysis compared costs with earnings from employment (Liberman et al. 1987), but the more interesting results came from the cost-effectiveness analysis (outcomes measured in terms of symptoms, social functioning and family functioning were crudely weighted into a single effectiveness index) (Cardin et al. 1986). A basic cost-offset analysis also found possible cost savings by family therapy (Goldstein 1996). This led the authors to conclude that family therapy was more cost effective than 'traditional individual-based management'.

Tarrier's economic study in Salford built on the previously reported benefits of a behavioural intervention with families of schizophrenic patients in terms of lower relapse rates (Tarrier et al. 1988; 1991). The evaluation found that any increased cost associated with the family intervention was outweighed by reduced utilisation of other mental health services. Other costs were not examined. Leff and colleagues (2001) confirmed this finding in circumstances where costs of training of staff were also

included in the analysis. In Norway, Rund (1994) reached a similar conclusion from a small sample of adolescent schizophrenia patients (n = 24), in a non-randomised trial. Costs were again measured quite narrowly.

Evidence from China (Xiong et al. 1994) comes from a randomised trial (n = 63) comparing standard post-hospitalisation care (which is effectively just a prescribed medication with possibly some outpatient contact) and family intervention. The latter was tailored to the complex family relationships and unique social environment in China, and involved monthly counselling on a range of topics, particularly management of social and work problems, medication, family education and crisis intervention. The 18-month RCT found that family intervention was associated with reductions in hospital re-admissions, duration of inpatient stay, duration of unemployment and family burden. There were also some advantages as measured using standard clinical scales. Both treatment costs and lost income from employment were measured, and the trial found lower costs for the family intervention group.

McFarlane (1995) et al compared two different ways of delivering family therapies, and demonstrated that a multi-family group intervention is more cost-effective than a single-family intervention. Compared to the weight of evidence on the atypical antipsychotics there is only a modest amount of economic data on family interventions. Most of the completed studies have some methodological weaknesses, but – notwithstanding the different approaches to family intervention studied – there appear to be grounds for believing that this kind of psychosocial therapy can be not only effective but also less costly than standard care. However, a word of caution is needed. Schooler and colleagues (1997) compared two types of family intervention - the form examined in some previous studies and a simpler version - and found no effectiveness differences between them, but similar to those found in earlier research. The research sites also practised 'an intensive and assertive clinic model … (and) an intensive family intervention may have been unnecessary' (Hargreaves 1998).

4.3 Care arrangements

Changing the hospital/community balance

The development of improved pharmacotherapies and psychosocial therapies has been one of the contributory factors in the shifting balance between inpatient and community-based care. It is by no means the only reason (Goodwin 1997). Communities have become more tolerant, and there is generally a better understanding of the needs and preferences of mentally ill people. Old psychiatric hospitals have become increasingly unacceptable, associated as they are with 'institutionalism' and restrictions on civil liberties.

Many high-income countries have seen quite marked reductions in the per capita numbers of in-patient psychiatric beds. The financing structure of some health care systems can generate resistance to changes in the hospital-community balance (such has been the experience in Germany, France, Belgium and the Netherlands). As we noted above, the high per diem costs of in-patient care provide another explanation for moves to reduce the number of hospital beds in favour of what are sometimes thought to be cheaper alternatives in the community. On the other hand, good quality community mental health care often requires support services from a range of agencies. What, then, is the economic evidence on community-based care?

There have been few studies of community care compared to hospital care that concentrate exclusively on people with schizophrenia or psychosis. Most studies have

looked at a range of diagnostic groups, and although schizophrenia is often the most common condition, the findings from these studies should be seen as providing fairly broad indications of the consequences of changing the locus of care specifically for people with schizophrenia.

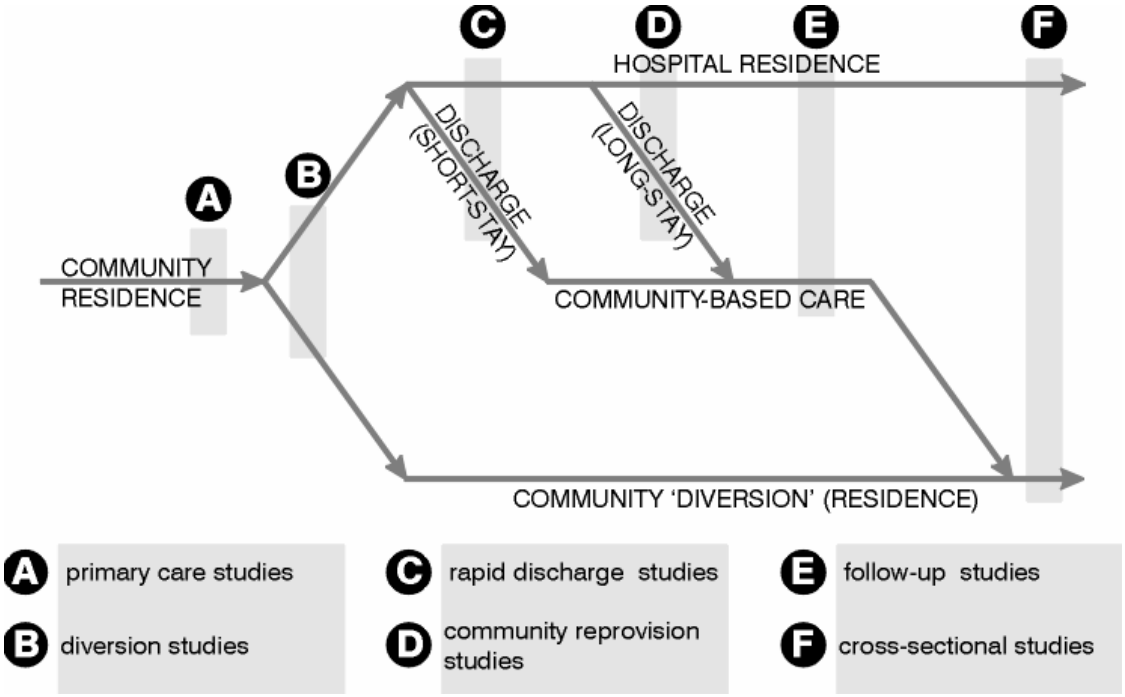
Many high-income countries share a common pattern not just of de-hospitalisation (policy and/or practice) but also of associated professional and public concerns. In the initial years of hospital rundown and closure, the focus has tended to be on whether and how long-stay, chronically ill residents of the facilities could move to community settings. Financial transfers have often been contentious issues, and new modes of inter-service and inter-agency coordination have had to be established. In some countries case management has been encouraged, although not always made available to these kinds of patients. Misgivings have been expressed in some professional and public quarters about hospital closures and the policy of community rehabilitation, but criticism of community-based care for long-term mentally ill people has generally dissipated as it has become apparent that most long-stay hospital residents are able to move successfully to the community (see below).

It is people who are acutely ill rather than chronically ill people who generate most concern. Patients with recurring florid symptoms of schizophrenia, it is often argued, are a danger to themselves and to others. They face ridicule and stigma. They may loose contact with their families, become destitute and homeless. They may fail to take their medications or to turn up for outpatient appointments. As psychiatric bed numbers are reduced, they may find it harder to gain admission, or to remain in hospital for as long as they really need. New care arrangements for acutely ill patients such as crisis interventions and acute day hospitals have been introduced.

One of the pressing questions of today in many mental health systems, therefore, is how to build up effective community-based services that can provide continuous, high-quality support. In many countries attention has turned to care arrangements such as the assertive community treatment model, various forms of case management and community mental health teams. The economic evidence on these is discussed below.

Figure 2 gives a highly simplified representation of a mental health care system, showing stylised routes through community and hospital-based services. Imposed upon the diagram are six broad types of research study. It is immediately clear that even a highly simplified model of a care system and a short selection of potential research studies suggest a large research agenda. Not surprisingly, the ratio of completed to potential economics research is rather low: relatively little formal evidence has yet accumulated. What evidence there is tends to be scattered across the diagram. The evidence is often robust, but it is clearly context specific (Creed et al. 1997; Dickey et al. 1986; Endicott et al. 1978; Fenton et al. 1982; Knapp et al. 1997b; Linn et al. 1979). However, there are two specific areas where evidence has come together in sufficient quantity to allow conclusions to be drawn: (a) community provision for former long-stay hospital residents; and (b) intensive community support for people with acute illnesses who would otherwise face hospitalisation.

Figure 2:



We focus the remainder of this section on these two fields. We should emphasise again that most studies cover people with a range of metal health problems, generally not being restricted to schizophrenia.

Community provision for long-stay inpatients

The changing hospital-community balance has obviously been one of the major themes of recent times and in large part has been achieved by relocating long-stay in-patients to suitably staffed community facilities. The controversy surrounding this often enforced rehabilitation and the practical difficulties of building or converting care facilities in the community have made it very difficult for researchers to set up randomised trials in this area. Consequently most economic, clinical and social evaluations have had to exercise imagination and caution in designing and interpreting empirical studies. One challenge, for example, is the tendency for hospital closure programmes to move the most independent, least symptomatic people first (Dorwart 1988; Jones 1993), requiring adjustments to be made to outcome and cost findings before generalisations are possible (Knapp 1996).

Many studies of the rehabilitation of long-stay inpatients have found community-based care to be more cost-effective than hospital care for most people, such as in the USA (Murphy 1976; Rothbard et al. 1999; Wright et al. 1997), Canada (Cassell et al. 1972), the UK (Beecham et al. 1997; Donnelly et al. 1994; Knapp et al. 1992) and Germany (Salize & Rossler 1996). This result applies particularly to those with less severe mental illness or fewer dependencies (Knapp et al. 1995). However, many long-stay inpatients with very challenging needs are more costly to accommodate in the current range of community settings than in hospital, even though their clinical and social outcomes do show improvements. Success depends on having sufficient staffing intensity (Trieman & Leff 1996); that is, it depends on expending sufficient costs.

The most comprehensive and long-running (10-year) evaluation of community-based care for former long-stay inpatients looked at the closure of two North London hospitals (Leff 1997). The outcome findings suggested that former inpatients were

enjoying a quality of life at least as good as in hospital 1 and 5 years after discharge (initially this was by comparison with matched controls in hospital, but later became a mirror-image design). There were no problems with higher-than-normal mortality, or with homelessness and crime. Accommodation stability in the community was impressive, and researchers and residents rated care environments as much better than hospital. Social networks were stable; a minority gained in this respect, but most were not socially integrated into local communities. Hospital readmissions were common (38% had at least one readmission over a 5-year period). Careful examination of clinical outcomes revealed striking stability over time in both psychiatric symptoms and social behaviour. Patients strongly preferred community living to hospital.

The associated economic evaluation found that many services were used in the community, with patterns of service use changing over time. The full costs were no different between community and long-stay hospital care (Beecham et al. 1997). Pooling the cost and outcome findings suggested that community care was more cost-effective. Higher cost community care packages appear to be associated with better individual outcomes. Care appeared to be more cost-effective in the public than in the private sector (Knapp et al. 1999).

Intensive community support

A vast number of models of intensive, community-based care have been developed and implemented across the world, all with the intention of supporting people with acute mental health problems outside inpatient settings if possible, but facilitating hospital admissions when appropriate. This wide range of models has been given a bewildering array of names, with unhelpful terminological inexactitude. Recent reviews of evidence on effectiveness and cost-effectiveness have rightly bemoaned the looseness with which labels have been attached to models, with the potential to confuse and unwittingly mislead decision-makers (Burns et al. 2001; Catty et al. 2002; National Collaborating Centre for Mental Health 2002). These reviews have also worked carefully through the evidence and sought to employ a more robust framework to organise it. One review grouped all services aiming to treat patients outside the hospital under the single heading of 'home treatment' arguing, 'the lack of a clear definition of different community-based models undermines any attempt to evaluate specific services through meta-analysis' (Catty et al. 2002 p.384). Notwithstanding that argument, with which we have great sympathy, we will here nevertheless describe the economics evidence under three heads: assertive community treatment, case management and community mental health teams. It should be borne in mind; however, that the models discussed under each of these headings will vary. It should also be emphasised that, in this area as much as in any other, evidence collected in one health system may not generalise well to another (Burns et al. 2002). A review of the economics evidence revealed once again that quality limitations hamper the ability to generalise from the accumulated evidence (Healey et al. 2004). Individual studies are discussed below.

Assertive community treatment

The assertive community treatment (ACT) or assertive outreach model associated with developments in Madison, Wisconsin has been one of the most important approaches in community psychiatry (Marx et al. 1973):

> ACT provides a comprehensive range of treatment, rehabilitation, and support services through a multidisciplinary team based in the community. Basic characteristics of ACT programs include assertive engagement, in vivo delivery

of services, a multi-disciplinary team approach, continuous responsibility and staff continuity over time, caseloads with high staff-to-client ratios, and brief but frequent contacts (high service intensity) (Scott & Dixon 1995).

The ACT approach has been quite widely copied across the world, although outside the USA usually only in demonstration sites (De Cangas 1994; Preston & Fazio 2000). Where evaluations have been conducted they have usually concluded that the approach can significantly improve outcomes (Mueser et al. 1998; Scott & Dixon 1995), although this is not always the case (Chamberlain & Rapp 1991; Holloway & Carson 1998). What are the economic consequences?

The original Training in Community Living model can be seen as a variant of ACT. It was evaluated in a cost-benefit framework (Weisbrod et al. 1980). Patients (n = 130) were randomly assigned to either the experimental community programme or to inpatient hospital treatment and community aftercare. Over 14 months, a range of input costs (spanning hospital, social services, criminal justice, social security services, plus informal carers foregone earnings) were compared to the monetised benefits of care (patient earnings). The additional benefits of the experimental programme ($1200 per patient year) were greater than the additional costs incurred ($800 per patient year), providing a clear cost-benefit advantage. Non-monetised indicators of patients' mental health (symptoms and satisfaction) were also significantly better in the community group.

A London modification of the ACT model - the Maudsley's Daily Living Programme (DLP) - looked at seriously mentally ill people facing crisis admission to the Maudsley Hospital. A randomised controlled trial recruited 189 people, many of them with schizophrenia. The DLP produced better outcomes, higher patient and family satisfaction and lower costs than standard care in the short term (Knapp et al. 1994; Marks et al. 1994), but after 4 years all of the earlier clinical gains and the cost advantage to the community programme were lost (Audini et al. 1994; Knapp et al. 1997b). Nevertheless, over the full 4-year period the DLP was more cost-effective than the standard hospital-based care with which it was compared.

Other studies confirm the cost-effectiveness of community-based crisis interventions, which may be seen to have ACT-like characteristics (Fenton et al. 1984; Ford et al. 2001). Although a multi-centred study in the US found discrepancies between the cost-saving characteristics of the different sites (Bond et al. 1988), the overall weight of evidence is that forms of ACT that adhere more closely to the original Wisconsin model are more cost-effective than conventional hospital-based services or other community arrangements (Catty et al. 2002; Essock et al. 199; Hoult & Reynolds 1985; Marshall & Lockwood 1998; National Collaborating Centre for Mental Health 2002; Santos et al. 1988; Test et al. 1985). Research has also begun to examine the patient characteristics associated with greater cost-effectiveness (Hoult & Reynolds 1985).

Case management

Moving away from the assertive outreach model, the organisation of community care generally could have a bearing on cost-effectiveness. Of especial interest has been the general theme of case management – which generally does not involve multi-disciplinary teams. In the case of the intensive form of case management, caseloads are small, as in the assertive community treatment approach. The efficiency evidence is equivocal. There are etymological and organisational difficulties that partly explain why it is difficult to reach firm conclusions (Burns 1997), and there are rather

different research designs. Some studies find variants of case management to be effective and cost-effective (McCrone et al. 1994; Quinlivan et al. 1995), whilst others do not (Ford et al. 1997). When comparing the cost-effectiveness of the standard and intensive forms of case management, two studies found standard form to be more cost-effective (Galster et al. 1994; Johnston et al. 1998). However, a large randomised controlled trial in the UK showed the two approaches to be equally cost-effective, and confirmed that reduced caseloads have no clear beneficial effect on the efficiency of case management (Byford et al. 2000).

Community mental health teams

Service provision by community mental health teams is well represented by the care programme approach (CPA) in the UK, which promises close supervision by nominated key workers from a multidisciplinary team. Compared to standard care, contact is more likely to be maintained with vulnerable patients under the CPA, but psychiatric inpatient admissions have been found to be higher (Tyrer et al. 1995). Another study compared CPAs administered by community-based and hospital-based teams following discharge from inpatient care, finding higher costs for the latter without any difference in outcomes (Tyrer et al. 1998). However, the high use of placements in private hospitals in one locality confounded the findings. Other studies of community mental health teams give equivocal results (Burns & Raftery 1993; Gater et al. 1997; Merson et al. 1996; Tyrer 1998) and the overall evidence suggests no real cost savings by this form of care arrangement (National Collaborating Centre for Mental Health 2002).

Numerous studies have compared the cost-effectiveness of the different community care arrangements, but no firm conclusions can be drawn about the superiority of one setting over the others since the evidence is neither unambiguous nor robust (Healey et al. 2004; National Collaborating Centre for Mental Health 2002).

Looking across the range of experiences, Tyrer (1988) concluded that:

> the exact model of community care being offered, whether assertive, intensive or standard, is really unimportant. The key to the success lies in having a coordinated team approach to the care of the severely mentally ill in which each member has the requisite skills to intervene appropriately and at an opportune time to produce the maximum benefit. Supporting the team's skills is therefore more important than reducing the case loads of individual workers. Our preoccupation with the bureaucracy of care - case load size, care programme levels, independent needs assessment - has prevented us from examining the more difficult task of what makes a team function badly or well, or in another sense, what allows it to be effective and assertive even if relatively deprived of resources.

4.4 Interventions for bipolar disorder

Two industry-sponsored studies from the United States have assessed the economic implications of olanzapine for patients suffering from mania. In a pre-post study, Namjoshi (2002) concluded that compared to the year prior to treatment olanzapine resulted in improved quality of life and reduced costs for 76 patients. However, given the lack of a control group (beyond the first 3 weeks of the study) it is unclear whether these patients would have improved anyway, or whether their gains were any greater due to olanzapine treatment. In the other study, Revicki (2003) did use a double-blind randomised design in their comparison of olanzapine with divalproex. Quality of life

deteriorated for both groups over a short 12-week period. Costs for outpatient care were significantly higher for the olanzapine group but this was due to the cost of medication. Overall health care costs were not significantly different, but this was largely because the sample all started off as inpatients and these costs dominated all others. Societal costs were not included. This study was limited by the small sample size (which was reduced further by the lack of follow-up data in a large proportion of patients).

A study of ECT for treatment-resistant bipolar disorder in adolescents and young adults found that outcomes were significantly better for those receiving ECT compared to those who declined it (Kutcher & Robertson 1995). Hospital costs were less for the ECT patients due to a much shorter length of stay. However, this was not a randomised comparison and the group willing to undergo ECT may have shown more improvement anyway. In addition, the sample size was very small.

In a retrospective case note study, Conney and Kaston (1999) compared the resource costs and adverse events associated with divalproex and lithium used in the treatment of nursing home residents with bipolar disorder and/or dementia. Although the acquisition costs of divalproex were substantially higher, the overall costs over two years were $2875 less per person compared with lithium and there were fewer adverse effects.

The relationship between health care costs and treatment outcomes was explored in a United States study (Bauer et al. 2001). The sample consisted of patients attending VA clinics. This was not a cost-effectiveness analysis as there was no comparison of alternative treatments and no a priori hypothesis that certain inputs would result in particular outcomes. It was of interest that the authors found no relationship between outcomes and costs.

A recent study conducted at the Institute of Psychiatry in the UK has evaluated cognitive behavioural therapy in comparison to usual care for the treatment of bipolar disorder. A comprehensive range of health and social care costs have been measured and combined with data on clinical outcomes and bipolar-free days using the net-benefit approach. The results of this study are expected in 2004.

4.5 Conclusions

The accumulated economic research provides consistent evidence on some fronts. For the full range of serious mental illnesses, and particularly for schizophrenia, arrangements have been developed for community-based care that has proved cost-effective. Examples would be the assertive community treatment model and the well-planned community rehabilitation of people who would otherwise remain for years in psychiatric hospitals. Evidence on two psychological approaches to treatment is also consistent in pointing to the potential for cost-effectiveness advantages. Family interventions appear capable not only of improving clinical profiles and reducing family burden, but also reducing the overall costs of care, and a short counselling intervention has been found to improve adherence with medication plans and clinical outcomes whilst not costing any more than standard care. Most people with schizophrenia live in community settings, not in hospitals. We still know very little about the cost-effectiveness of the different organisational arrangements for community care.

The arrival of atypical antipsychotic drugs has generated a lot of new economics research. For clozapine the accumulated weight of evidence points to a cost-

effectiveness advantage over conventional neuroleptics. The cost-effectiveness of other atypicals is not so well established without ambiguity, and none has yet been the subject of as much economics research as clozapine. The balance of evidence appears to point to a cost-effectiveness advantage over conventional drug treatments in West European and North American health systems, but the accumulated evidence is not all in agreement with such a conclusion. It should be emphasised that the atypicals are not identical in their clinical effects, and we would not expect them to have exactly equivalent cost-effectiveness profiles.

Much remains to be researched. Many of the psychological approaches currently practiced have not been evaluated by economists, nor have the newest of the atypical antipsychotics. There have been very few head-to-head comparisons between two or more atypical antipsychotics. There is little evidence on the economic consequences of first-line treatment with atypicals. Another underdeveloped research area relates to the distributional (equity) consequences of different treatments and care arrangements.

5. EVIDENCE: DEPRESSION

Depression was the fourth leading contributor to the global burden of disease in 2000 and WHO projections estimate that it will have moved to second place by 2020. Depression not only places a financial burden on health and social services, but evidence consistently suggests that there is a large impact of depression on days lost from work and productivity losses (Crott & Gilis 1998). Because depression impacts on many areas of the health system and economy, it is important that evaluations of costs and outcomes take a wide cost perspective and include health service costs, social and non-statutory service costs, societal costs and costs to the individual. Unfortunately, evaluations that encompass all these costs are few and far between. Most published economic evaluations of depression treatment take a narrow cost perspective and are based on one of three research designs: mirror-image (before-after) comparisons; decision and Markov models constructed from a combination of observational (perhaps trial-based) evidence and expert opinion; and secondary analyses of naturalistic (often routinely collected) data. Prospective randomised trial evidence with an economics component – a fourth design, and generally much to be preferred, by the criterion of internal validity at least – is still quite rare. The lack of evidence from prospective randomised trials is most pronounced in the economic evaluations of pharmacological interventions.

Improving outcomes in depression is likely to influence costs as evidence suggests that there is a strong association between depression and health service utilisation (Simon & Katzelnick 1997). An improvement in symptoms may lead to fewer visits to health care professionals and perhaps reduce the need for an inpatient admission. In addition, depression has a high level of co-morbidity with other psychiatric disorders and physical conditions. Co-morbid depressive illness often prolongs and complicates treatment for a physical disease (Sartorius 2001). Effective intervention for depression may therefore improve both psychological and physical outcomes and result in lower levels of health service utilisation.

Treatment for most people with depression consists of antidepressant medication, psychotherapy, or both. This section of the report first reviews the evidence on pharmacotherapies, and then turns to psychological therapies and changes in care arrangements that may improve clinical outcomes.

5.1 Pharmacological interventions

Pharmacotherapy remains the mainstay of treatment for depression. Antidepressants are effective across the full range of severity of depressive disorders (Geddes et al. 2003). The widely used antidepressant drugs fall into three types: tricyclic and related antidepressants (TCAs) which include amitriptyline, dosulepin and imipramine and trazodone; the newer selective serotonin re-uptake inhibitors (SSRIs) which include citalopram, fluoxetine, fluvoxamine, paroxetine and sertraline; and other new preparations including mirtazepine, venlafaxine and nefazodone. Systematic reviews that compare available evidence on the efficacy of different antidepressants have found that there are no significant differences in outcomes between the different kinds of antidepressant drugs (Geddes et al. 2002; 2003; Song et al. 1993).

Assuming similar efficacy, the relative cost-effectiveness of antidepressants is therefore determined by a number of factors. Firstly, the SSRIs and other newer antidepressants have a considerably higher purchase price than the TCAs and higher drug costs can lead to higher total costs. However it is unclear how long this trend will continue as newer antidepressants are now coming off patent and can be sold generically at a much lower price: in March 2000 a 30-day supply of fluoxetine (Prozac) in the UK was £19.34 but by September 2003 the equivalent generic fluoxetine was £6.83. Secondly, patient adherence is low and dropout rates high among individuals commencing antidepressant treatment, which impacts on the effectiveness of the drug. One possible explanation is the unpleasant side effects associated with the drugs; these include as dry mouth, sedation and blurred vision. It is considered that SSRIs have a better side-effect profile than the TCAs and this feature of the newer preparations may improve adherence and outcomes. Economic evaluation is therefore concerned with whether the increased treatment costs of the newer antidepressants are justified in terms of increased benefits or savings realised elsewhere in the health system or in society.

Selective serotonin re-uptake inhibitors

Beginning with higher quality evidence, economic evaluations using data from prospective or naturalistic settings are relatively rare. We identified only one, a prospective, naturalistic, randomised trial with economic evaluation that compared alternative antidepressant therapies (Simon et al. 1996; 1999). Patients initiating antidepressant treatment attending primary care clinics in the US were randomised to fluoxetine (an SSRI) or desimpramine or imipramine (TCAs). Results suggested that in the short-term (six-months) treatment dropout was lower, there were fewer adverse effects, and achieving a therapeutic dose was more likely among patients randomised to receive fluoxetine. There were no significant differences in clinical outcomes or quality of life, nor were there any significant differences in cost, because the higher drug acquisition cost of fluoxetine was offset by lower outpatient and inpatient service use. Similar results were found at the two-year follow-up. The authors concluded that restrictions on first line use of fluoxetine in primary care would probably not reduce overall treatment costs due to lower hospital service utilisation in that group. Despite the fact that the trial was not controlled and participants were free to change medication, the results are applied to decision-making as they more accurately reflect routine care.

Two RCTs were identified which compared SSRIs with other antidepressants and with psychological therapies. One study compared the costs and outcomes of fluoxetine, citalopram and amitriptyline for major depression in the Czech Republic, Europe and Central Asia and found no significant differences in cost or outcome

(Hosak et al. 2000). The authors concluded that amitriptyline was no less expensive or more effective than citalopram or fluoxetine and advised that there was no advantage to restricting patients from treatment with SSRIs.

A second study compared SSRIs, placebo and psychological treatment for common mental disorders including depression in Goa, India (Patel et al. 2003). Psychiatric outcomes were significantly better with antidepressant than placebo at two months but no significant difference was detected at 12 months. Costs were lower in the SSRI group, suggesting that antidepressants are more cost-effective than placebo. Psychological treatment resulted in worse outcomes and higher total costs than placebo. The authors argued that affordable antidepressants such as fluoxetine should be the treatment of choice for common mental disorders in general health care settings in India, since they are associated with improved clinical and economic outcomes, particularly in the long-term.

Retrospective analysis of existing data was used to measure the cost-effectiveness of sertraline and TCAs for depression in primary care in the UK (Forder et al. 1996). The average cost of treatment was slightly greater for those receiving TCAs due to greater use of psychiatric services. In terms of cost-effectiveness, sertraline was found to dominate TCAs for all definitions of costs and outcomes.

Thus, evidence from RCTs tends to suggest that SSRIs are a more cost-effective treatment for depression than TCAs. Despite higher acquisition costs, SSRIs do not appear to increase overall treatment costs as a result of reductions in subsequent health service utilisation. In addition, SSRIs tend to generate better outcomes.

In comparison to the limited availability of economic evaluations from naturalistic settings and RCTs, there is a plethora of studies that use modelling techniques to estimate the cost-effectiveness of different treatments for depression. The Markov and decision models use data from existing evidence and expert opinion and are based in a variety of health systems and settings.

A decision-analytic model was used to analyse the cost-effectiveness and cost-utility of SSRIs and TCAs in various combinations for major depression in Canada and is a good overview of the evidence of the relative cost-effectiveness of the two types of antidepressant (Canadian Coodinating Office for Health Technology Assessment 1997). The meta-analysis of available clinical evidence showed that there are no statistically significant differences between the efficacy, completion rates and dropout rates of the antidepressants considered. The perspective of the economic evaluation was that of the health care system so only direct health care costs were included; the incremental cost of the SSRI/TCA v TCA/SSRI strategy was $2,818 per QALY. The study suggests that both TCAs and SSRIs should be part of an effective treatment strategy and that further research, preferably from RCTs is needed to investigate the long-term cost-effectiveness of treatment for major depression.

Jönsson and Bebbington (1994) compared the cost-effectiveness of paroxetine (an SSRI) and imipramine (a TCA) in people with depression in the UK. The 12-month cost per successfully treated patient was lower with paroxetine than imipramine indicating that paroxetine is a preferable treatment. The results were sensitive to assumptions concerning the relative efficacy of the drugs, particularly treatment failure, and the authors concluded that although paroxetine had a high cost per day when patient adherence and the total cost of treatment are taken into account it was the more cost-effective outcome. However, these findings were questioned in 1997 when the model was reassessed with some key assumptions challenged and changed

(Woods & Rizzo 1997). With revised assumptions the model demonstrated that the TCA was at least equally if not more cost-effective than the SSRI. The authors advised that a policy of using TCAs as a first choice antidepressant with SSRIs reserved for those patients not doing well appears more cost-effective than the reverse sequence. The two studies use the same data but generate different results, confusing the issue of cost-effectiveness and highlighting the importance of the assumptions made in economic models.

In another UK model, Stewart (1994) explored the cost-effectiveness of SSRIs and TCAs for major depression. The average annual cost per successfully treated patient was lower for imipramine and amitriptyline (TCAs) than for sertraline and paroxetine (SSRIs). Stewart concluded that there was no clear cost advantage in switching from TCAs to SSRIs. The model was updated and the incremental cost of the SSRIs per successfully treated patient was reduced advocating the general use of SSRIs (Stewart 1996).

In France, treatment with fluoxetine (an SSRI) induced short-term societal cost savings among those with mild to moderate depression due to reduced treatment dropout (Le Pen et al. 1994) and in recurrent depression, fluvoxamine (an SSRI) was both less costly and more effective than TCAs (Nuijten et al. 1998).

The cost-effectiveness of SSRIs as a maintenance therapy has been examined in three modelling studies that engender different results. In the first study the lifetime health and economic impact of maintenance therapy with sertraline (an SSRI) and episodic treatment with a TCA for depression was estimated. Maintenance treatment with sertraline elicited a cost per QALY of £2,172 (Hatziandreu et al. 1994). In the second study, health status and economic outcomes were estimated over a one-year follow-up period, for patients with major depression. Citalopram, (an SSRI), was both more effective and less costly than standard therapy (a TCA) and therefore dominated in terms of cost-effectiveness (Nuijten et al. 1995). In the third study, the prophylactic use of SSRIs in patients with a known history of depression resulted in a higher cost per symptom free patient than a 'watch and wait' to treat approach (Kind & Sorensen 1995).

SSRIs have demonstrated both treatment dominance and incremental cost-effectiveness as maintenance therapies. However, ambiguities remain as a result of differences in the model assumptions made by the authors. Thus, on the basis of available evidence, it is not possible to recommend SSRIs as a maintenance treatment in recurrent major depression.

Other newer antidepressants

More recently, newer antidepressants have entered the market; these include venlafaxine, nefazodone, mirtazepine and milnacipran. In common with evidence of the cost-effectiveness of SSRIs, decision and Markov models dominate economic evaluations for the newer antidepressants. We know of only one study that prospectively collected and analysed data on cost-effectiveness. This study focused on mirtazepine versus paroxetine in UK primary care attenders with depression (Romeo et al. 2004b). Mirtazepine treatment resulted in significantly greater improvements in quality of life than paroxetine at 26 weeks. Although no significant cost differences were observed between the two groups, mean total societal costs were lower with mirtazepine than with paroxetine. The results suggest that mirtazepine may be a cost-effective treatment choice for depression in a primary care setting.

The following economic evaluations for the newer antidepressants are all based on data-analytic models. The cost-effectiveness of venlafaxine for major depressive disorder has been estimated using models in a number of health care systems. Doyle and colleagues compared venlafaxine and other antidepressants in ten countries: Germany, Italy, Netherlands, Poland, Spain, Sweden, Switzerland, UK, United States and Venezuela (Casciano et al. 2001; Doyle et al. 2001). Using results from meta-analyses, venlafaxine had the highest expected success rate and the greatest number of symptom-free days in all countries. It yielded a lower expected cost in all countries except Poland in the inpatient setting and Italy and Poland in the outpatient setting. The authors concluded that venlafaxine is a more cost-effective treatment than the alternatives and suggest that increased utilisation of the compound in most settings across Europe and the Americas will have favourable impacts on health care payer budgets. The model was re-analysed when new data became available on the probability of relapse with different antidepressants (Casciano 2003). The revised study disputed the treatment dominance of venlafaxine and concluded that venlafaxine was in fact more expensive and more effective than SSRIs.

The cost-effectiveness of venlafaxine for people in the acute phase of major depressive disorder was evaluated in a UK outpatient setting (Freeman et al. 2000). The model demonstrated that venlafaxine offered statistically significant improvements in depression-free days and from a health care perspective, the cost per depression-free day was lower for venlafaxine than for SSRIs or TCAs. A similar evaluation was undertaken in Italy (Casciano et al. 1999). The results suggested that venlafaxine was more cost-effective compared to SSRIs and TCAs for both inpatients and outpatients with respect to cost per successfully treated patient and cost per symptom-free day.

Finally, venlafaxine for people with major depressive disorder was evaluated in two models which demonstrated the cost-effectiveness of the preparation in both inpatient and outpatient settings in Canada and the US (Einarson et al. 1995; 1997). Results from both studies suggested that venlafaxine was more effective, but in one study venlafaxine was less costly and in the other it was more costly than other antidepressants. The results of all the models above are highly sensitive to the assumptions made and the unit costs used. At present, and on the basis of available evidence, it is not possible to make a judgement on the cost-effectiveness of venlafaxine for depression.

Two models have evaluated the cost-utility of nefazodone in depression, from the perspective of a US managed care organisation (Revicki et al. 1997) and a Canadian health insurance organisation (Anton & Revicki 1995). In both models, cost-effectiveness was estimated for a 30 year-old woman with active depression and in both studies the findings suggested that nefazodone is a cost-effective treatment compared with imipramine (a TCA) or fluoxetine (an SSRI). The results were highly sensitive to the assumptions made in the model, particularly those concerning efficacy and dropout.

Mirtazepine for people with moderate to severe depression has been investigated in the UK and Austria. In the UK study Borghi and Guest (2000) demonstrated that mirtazepine was both more effective and less costly when compared to amitriptyline and fluoxetine. The higher acquisition costs of the preparation were offset by the lower costs of managing adverse events and lower health service utilisation. In Austria, Brown and colleagues (1999) established the cost-effectiveness of mirtazepine when compared to other antidepressants.

Newer antidepressants have entered a crowded market, and except in one instance real-life comparisons to existing antidepressants have not yet been undertaken. In common with the evidence from other Markov and decision-analytic models, it is difficult to summarise the cost-effectiveness of these interventions. In many cases, the models relied entirely on expert views to project the costs, and the precise methods used by the expert panels to arrive at their resource use estimates are not described fully and clearly in the literature. These inadequacies limit the generalisability and applicability of these studies and make it difficult to draw firm conclusions.

5.2 Psychological interventions

In contrast to the pattern of evidence on the cost-effectiveness of pharmacological interventions, there are a number of good quality economic evaluations of psychological therapies for people with depression, in a number of different treatment settings. Psychological therapies include cognitive behavioural therapy (CBT), counselling and psychotherapy. These interventions usually have high treatment costs because they are intensive, individual therapies administered by qualified professionals. Psychological therapies have proven effectiveness in depression (Geddes et al. 2003), so economic evaluations aim to investigate whether high initial treatment costs are offset by potentially lower drug costs and fewer visits to other health care professionals or if the additional costs are worth paying because of improved outcomes.

Counselling

Counselling is a psychological treatment that aims to help the patient work out his or her problems. The role of the counsellor is to listen sympathetically, identify with the problem, clarify difficulties and sometimes give advice.

The review of the evidence begins with four cost-effectiveness analyses and one meta-analysis from the UK. No significant differences in costs or effects were found between psychodynamic counselling and usual care in one study, although fewer patients at follow-up were classified as 'cases' in the counselling group at follow-up (Simpson et al. 2003). Harvey and colleagues confirmed these results, concluding that there was no evidence that counselling in primary care is more effective than usual GP care in treating a wide range of mental health problems including depression (Harvey et al. 1998). Clinical results demonstrated no significant differences so a cost-minimisation analysis was used to compare counselling and usual care in general practice in the third study (Friedli et al. 2000). Over the nine-month follow-up period the counsellor group remained more expensive per patient compared with the general practitioner (GP) group. In the fourth study, counselling, CBT and usual GP care were compared in a three-arm cost-effectiveness analysis (Bower et al. 2000). All clinical outcomes were equivalent at 12-months follow-up and there were no significant differences in direct costs, productivity losses or societal costs between the three treatments at four and 12 months follow-up. Thus there is no evidence to suggest that counselling was more or less cost effective than usual care in the long run.

The findings from all four studies must be considered preliminary given the likely low statistical power of the cost data. In an attempt to overcome these sample size limitations, Bower and colleagues (2003) undertook a meta-analysis of data on costs. The meta-analysis included individual patient data from the four trials, and demonstrated that each study was under powered to produce useful conclusions about the cost comparisons. Incremental cost-effectiveness over the short-term was £150 per point improvement on the Beck Depression inventory (BDI), and over the long-term

£196 per point improvement on the BDI. The uncertainty surrounding the cost-effectiveness ratio was explored using cost-effectiveness acceptability curves that showed - for willingness to pay values above £196 - that counselling had a greater than 50% probability of being cost-effective compared with usual GP care. The results of the analysis are sensitive to assumptions made about the cost of sessions with a counsellor and the management of patients by a general practitioner.

More recently, Miller and colleagues (2003) used advanced health economic techniques to compare counselling and antidepressant therapy for the treatment of mild to moderate depression in primary care. At twelve months follow-up, there were no significant differences in outcomes and costs. Bootstrap analysis showed that for the majority of patients the antidepressant intervention was the dominant cost-effective strategy. The Miller study further supports the results of the meta-analysis; the cost-effectiveness of counselling for depression in primary care has not been proven.

Cognitive behaviour therapy (CBT)

CBT is widely used in psychological disorders including anxiety and depression and is based on the belief that such problems are the product of faulty ways of looking at the world. The role of the therapist is to assist the patient to identify these false ways of thinking and avoid them.

In an early economic analysis, 120 patients initiating treatment for depression were randomised to one of four interventions: CBT by a clinical psychologist, counselling and case work by a social worker, amitriptyline prescribed by a psychiatrist and usual care from a general practitioner (Scott & Freeman 1992). After 16 weeks, there were improvements in depressive symptoms in all treatment groups, but treatment total costs were twice as much in the specialist treatment groups compared to routine care. With such a short period of follow-up, it was difficult to draw conclusions and the authors recommended a full economic evaluation with longer follow-up and one that included a wider definition of cost.

A recent RCT from the UK explored strategies for the prevention of relapse in depression using CBT (Scott et al. 2003). CBT was found to produce significantly lower relapse rates than usual care for significantly greater costs. Cost-effectiveness acceptability curves were presented to depict the probability that CBT is more cost-effective than usual care for a range of minimum values a decision-maker would be willing to pay per relapse prevented. The paper is a high quality RCT and economic evaluation although the cost estimates included only health care costs excluding productivity and other indirect costs which if included could alter the relative cost effectiveness of the intervention. In addition, the calculations assumed that the benefits of CBT would all be realised within the study period, which may not necessarily be the case.

In another UK study, decision analysis was used to compare the cost-effectiveness of computerised CBT with usual care and results suggested an incremental cost of between £1,200 and £7,700 per QALY gained (Kaltenthaler et al. 2002). However, this figure was acknowledged to be a crude estimate based on limited data so the conclusions must be viewed tentatively.

Only one RCT from the UK has explored the cost-effectiveness of CBT for deliberate self-harm (Byford et al. 2003b). Brief CBT was compared to treatment as usual in a group of patients with recurrent deliberate self-harm. No statistically significant

differences in costs or effects were found at 12-months follow-up. But, using a decision-making approach, cost-effectiveness acceptability curves demonstrated that to reject the CBT in favour of treatment as usual had a less than 10% chance of being the correct decision in terms of cost-effectiveness.

The studies above suggest that CBT may be associated with improved clinical outcomes, but at a greater cost. Decision-makers must therefore decide if the improvement in outcomes is worth the additional cost. More advanced health economic techniques have been used to overcome the problems of small sample sizes and present to the decision-maker the probability that the CBT intervention is cost-effective.

Psychotherapy

Psychotherapy is the treatment of depression through individual and group interaction and its cost-effectiveness has been investigated in trials in Canada, the US and the UK. In one study, patients with dysthymia were randomised to interpersonal psychotherapy (IPT), IPT with sertraline (an SSRI) or sertraline alone in an RCT in primary care (Browne et al. 2002). Clinical outcomes at two-years follow-up demonstrated that there were no statistically significant differences between sertraline alone and sertraline plus IPT, but both were significantly more effective than IPT alone in reducing depressive symptoms. Societal costs were significantly lower in the IPT group, but there was no synthesis of costs and effects so the incremental cost-effectiveness of the treatment is not known. The authors stressed the importance and potential economic value of combining psychotherapy and pharmacotherapy.

IPT, pharmacotherapy with nortriptyline (a TCA) or usual care were compared in a cost-effectiveness analysis in the US (Lave et al. 1998). Both IPT and the pharmacotherapy provided better outcomes than usual care at follow-up although the pharmacotherapy group did slightly better than those assigned to IPT. Costs were higher in the IPT and pharmacotherapy groups compared to usual care. The incremental cost per QALY gained was US$11,695 for the pharmacotherapy and US$15,358 for IPT, indicating a decision-making preference for the drug treatment.

IPT was compared to usual care in patients with enduring psychiatric symptoms (including depression) in a psychiatric outpatients department (Guthrie et al. 1999). Patients receiving IPT had significantly greater improvements in levels of psychological distress and social functioning and significant reductions in the cost of health care utilisation excluding treatment costs at six months follow-up. During the intervention phase of the trial there were no significant differences in costs.

A modelled cost-utility analysis compared IPT, imipramine (a TCA) a combination of the two, with a placebo in patients with recurrent depression (Kamlet et al. 1995). A Markov model and Monte Carlo simulation were used to estimate the costs and benefits associated with each maintenance therapy and the authors demonstrated that the drug maintenance treatment was cost-effective.

Among patients with depression who had a partner with a criticising attitude, significant improvements in outcomes were found in patients randomised to couple therapy compared to those randomised to antidepressants (Leff et al. 2000). There were higher treatment costs in the therapy group, but the higher costs were moderated by decreased use of other services resulting in no significant differences in cost at follow-up. The authors warned that the results could not be generalised beyond individuals with depression who are living with a heterosexual partner and that

conclusions were limited by large amounts of missing data in the economic evaluation.

In common with the evidence on CBT for depression, psychotherapy may produce better outcomes but at an increased cost.

5.3 Care arrangements

Care arrangements can refer to either changes to the organisation of health systems, the professionals responsible for patient care or the system of managing and treating a depressive episode. Increasingly, care arrangements and care plans involve multi-disciplinary teamwork and service user engagement in treatment planning and in therapy.

Health systems

A multi-disciplinary parent and baby day unit was compared to routine primary care in women with postnatal depression (Boath et al. 2003). At six months follow-up there were significantly lower levels of depression, and higher costs in the day unit group. The cost-effectiveness of the day unit per successfully treated woman was lower than in the control group, supporting the adoption of the unit. The generalisability of the results however are limited by the highly specialist nature of the day centre, the small sample size and the narrow cost perspective. Despite these limitations, the authors recommend multidisciplinary parent and baby day units to decision-makers.

The cost effectiveness of a community mental health team compared to hospital based services for people with depression and anxiety was examined in a UK study (Goldberg et al. 1996). Clinical and social outcomes were similar in both groups but patients treated in the community were seen more quickly and were more satisfied with the care they received. Health service costs were less for patients in the community because they were less likely to have an inpatient stay and the authors concluded that treatment by a community team is more cost-effective than hospital care.

Nurses and support workers

Two studies considered the cost-effectiveness of nursing as a health care intervention for people with depression and related symptoms. The first studied the costs and effects of a public health nursing case management intervention on mood-disordered single parents on social assistance (Markle-Reid et al. 2002). At follow-up, there were clinically important but not significant improvements in social adjustment for the nursing intervention group compared with usual care. The nursing intervention also resulted in a higher use of all services, although there was no statistical difference in total societal costs at follow-up. The study suggests that it is no more costly proactively to provide a service to single parents with mood disorders on social assistance, however the very specific patient group included in the study seriously limits the generalisability of this study.

The second study was an economic analysis of a community psychiatric nurse (CPN) compared to routine GP care for patients with non-psychotic problems in primary care (Gournay & Brooking 1995). Improvements in depressive symptoms were seen in both groups over time, although differences in outcomes between the groups were not statistically significant. Total societal costs were higher in the usual care group

compared to the CPN group; the saving of resources was due to reductions in work absences. However, the authors based their conclusions on direct costs only, estimating the incremental cost of the CPN intervention as £28,000 per QALY.

Nurse training in mental health skills and care management evaluated in an RCT in the USA was found to be more effective and more costly than usual care for women, with an incremental cost of US$5,244 per QALY gained (Pyne et al. 2003). No such differences were observed for men, possibly due to the small numbers in the study (n=33). In a UK study, problem-solving treatment given by community nurses was compared to usual GP care for people with emotional disorders including anxiety and depression (Mynors-Wallis et al. 1997). There was no significant difference in clinical outcomes between groups on any measure, although patients who received problem-solving treatment had fewer disability days and fewer days off work. Analysis of health care costs revealed significantly higher costs but lower productivity losses in the treatment group over follow-up.

Schoenbaum and colleagues (2001) evaluated the cost-utility of a quality improvement programme for the treatment of depression in primary care. The programme involved offering training to practice leaders and nurses, enhanced educational and assessment resources and either medication follow-up by nurses or psychotherapy. Concluding that the estimated cost per QALY gained was within the range of many acceptable medical interventions, the authors noted that a strength of their study was the 'real world' context and naturalistic setting.

Morrell et al (2000) investigated the impact of additional support for new mothers on rates of post-natal depression. Comparing usual care by midwives to usual care plus post-natal support workers they found no differences in clinical outcomes, but significantly higher costs in the support-worker group. The authors concluded that there was no evidence in favour of the intervention.

The economic evaluations reviewed in this subsection suggest that involving nurses in primary care treatments for people with depression may improve outcomes, but that this improvement may take place alongside increasing costs.

Collaborative care and case management

Collaborative care models are being increasingly used and studied, particularly in the US. They are multifaceted interventions that include diagnosis and treatment, patient education, patient support and progress evaluation. Collaboration is usually between the primary care physician and other professionals and many models use nurses or non-clinical care managers as care planners. There is an emphasis on patient involvement and patients are often given a book or video explaining how medications and psychotherapy help depression and how they can play an active part in their treatment. Telephone feedback from care managers to both treating physician and patient is used to preserve the involvement of the different groups.

Four US-based RCTs have compared collaborative models to usual care for depression. Liu and colleagues (2003) found that there was a significant reduction in the number of depression-free days in the collaborative care group, but that it was associated with higher health service costs. Statistical bootstrap analysis suggested that there was a 97% probability that collaborative care was the more cost-effective option.

A second study demonstrated similar significant differences in outcomes in favour of collaborative care in those with moderate symptoms of depression (Katon et al. 2002a). Here there were no significant differences in cost and statistical bootstrap analysis suggested a 70% probability that collaborative care was more cost-effective.

In patients with persistent depression, patients receiving collaborative care demonstrated significant improvements in depression-free days (Simon et al. 2001a). Service use was higher in the intervention group and the greater cost of the care programme was attributable to greater expenditure on antidepressant prescriptions and outpatient visits. The probability that the collaborative care model was the more cost-effective option in this patient group was 98%.

Finally, von Korff and colleagues (1998) synthesised the results from two clinical studies to build a cost-effectiveness model of collaborative care for depression. Collaborative care management improved the number of successfully treated patients among those with major depression, but differences were not observed in those with minor depression. Among patients with major depression, the cost per patient successfully treated was lower for collaborative care than for usual care. Conversely, for patients with minor depression, collaborative care was more costly and not more cost-effective than usual care.

Three studies have investigated the cost-effectiveness of care management versus usual care in patients starting antidepressant treatment. Similar to collaborative care, care management tends to involve patient education, shared decision-making and monitoring, but there is less emphasis on inter-disciplinary care and co-operation. In two trials clinical outcomes suggest there are no significant difference in depression-free days or in health care costs (Simon et al. 2000; 2002). A decision-analytic model suggested that an increase in the appropriateness of care as seen in a care management programme is likely to improve functioning outcomes and increase the value of health care spending in terms of health benefits (Sturm & Wells 1995).

Collaborative care and case management appear to be effective interventions for improving outcomes in patients with depression. In many cases these improved outcomes are achieved alongside higher health service costs, although short study follow-up periods do not allow potential long-term cost savings to be registered. The Katon study (2002a) had a longer follow-up period than the other studies and long-run differences in cost between the intervention and control groups were not significant. Successful collaborative care and case management systems have often developed in health services over a period of time for a particular patient group, therefore due to the specialist nature of the intervention it is often uncertain how the results might generalise to other populations of patients.

5.4 Identification and screening

Evidence of undiagnosed depression has led to calls for routine screening for depression in primary care. An RCT to identify and treat depression among high users of primary medical care found that the intervention increased the probability of initiating depression treatment, increased the intensity of treatment and produced significant improvements in clinical and functional outcomes (Simon et al. 2001b). Costs were higher in the depression management group and the cost per QALY was estimated to be $49,500. The results are only applicable to a specific patient group of high users of medical care and the high costs may reflect the high level of service use among this group.

A Markov simulation model estimated the cost-utility of screening for depression in a US Health Maintenance Organisation (Valenstein et al. 2001). It was assumed that screening was undertaken using a self-administered depression questionnaire with additional nursing assessment. From the perspective of the health care payer and society, the cost per QALY of annual screening and one-off screening was $192,444 and $32,909, respectively. The high costs per QALY varied in sensitivity analysis but low estimates were highly dependent on low screening costs and implausibly low rates of remission.

On the basis of available evidence, it does not appear that screening for depression in a primary care environment is a cost-effective option.

5.5 Conclusions

The economic evidence reviewed in this section does not paint a clear or unambiguous picture. There are a number of reasons. Firstly, results from clinical trials are frequently inconclusive due to short follow-up periods and inadequate power to demonstrate differences in costs. Secondly, the results from economic models are strongly influenced by the assumptions made; in many cases conclusions have changed when new evidence has become available or when a different view is taken on the likelihood of an assumption. However, bearing in mind these features of the economic evaluations, it is possible to identify some trends in the results and also to identify areas where further research is needed.

Evidence establishing the cost-effectiveness of SSRIs is accumulating. Many studies have demonstrated that SSRIs have higher acquisition costs but lower subsequent health service costs, a pattern that may be repeated as more SSRIs become available generically at a cheaper price. On balance, the other newer antidepressants nefazodone and venlafaxine appear to be cost-effective alternatives to other antidepressants, although the findings are based solely on results from models and not data collected from prospective studies.

Despite the availability of better quality evidence for the cost-effectiveness of psychotherapies, their cost-effectiveness (or cost-ineffectiveness) is yet to be established. An explanation for the inconclusive results is the fashion for economic evaluations to be tagged onto clinical trials, where sample size is based on the power calculations to establish significant differences in outcomes rather than differences in cost, which may well require much larger numbers of participants. In addition, many studies included a narrow definition of cost, choosing to include only health care costs, which may not have picked up the impact that the intervention had on other areas such as employment and productivity.

The cost-effectiveness of counselling as an alternative to usual care has not yet been proven, but it is generally no more expensive than usual care in the long run, and clinical outcomes are much the same. CBT was found to be more effective and more costly than usual care, necessitating examination of the willingness to pay for an improvement in effectiveness. Psychotherapy is cost-effective in some patient groups, but when compared to antidepressants, the medication treatments tend to demonstrate treatment dominance. The economic value of combining psychotherapy with pharmacotherapy needs further examination.

Studies of nursing interventions established some improvements in outcomes but usually at a higher cost. Collaborative care and case management produced better outcomes at higher costs.

Finally, care arrangements have demonstrated effectiveness but studies have only taken place in the USA and, given the fundamental differences in health systems across the world, it is not possible to generalise these results beyond North America.

6. EVIDENCE: ANXIETY DISORDERS

Accumulating evidence has established the high prevalence of a range of anxiety disorders. Many of these cause notable distress and significantly impair the daily activities of sufferers. Additionally, such disorders are commonly associated with more severe mental health problems such as depression. People with anxiety disorders are therefore likely to need a number of health and other support services. Although there have been a rising number of cost of illness estimates for different anxiety disorders, all pointing towards the substantial economic burden they place upon society, there is relatively little evidence on treatment patterns and the cost-effectiveness of specific treatment approaches. Indeed, some anxiety disorders (such as social phobia) have only relatively recently been included as separate diagnoses in their own right in diagnostic classifications such as DSM. A search of the literature covering the last two decades on anxiety disorders overall and individual anxiety disorders (generalised anxiety disorder, social anxiety disorder/social phobia, phobic disorders, post-traumatic stress disorder, panic disorder, obsessive-compulsive disorder, agoraphobia and somatoform disorder) revealed only a handful of formal economic evaluations. However, there was a promising trend towards greater discussion of economic issues in the treatment of anxiety disorders, and several cost-offset evaluations.

Given the lack of cost-effectiveness evidence in this area, we review any cost-effectiveness evidence identified and additionally other evaluative evidence/reviews that highlight economic issues in the treatment of anxiety disorders.

6.1 Panic disorder

One-year and lifetime prevalence estimates for panic disorder in the US general population have been reported at 2.3% and 3.5% respectively (Kessler et al. 1994). As the disorder commonly manifests itself as multiple medically unexplained symptoms, it is commonly associated with high rates of service use. Therefore, higher prevalence rates have been suggested for general medical settings (Ballenger 1998).

Katon (2002b) noted the severe nature of the disorder and the lack of evidence-based treatment of it, and reported one of the few full economic evaluations in this area. They conducted a cost-effectiveness analysis of a collaborative care intervention for primary care patients, which involved increased patient education and integrating a psychiatrist into primary care. 115 patients were randomised to either the intervention or to usual care. Service use, costs and anxiety-free days over a 12-month period were compared. Patients receiving the collaborative care intervention reported an average of 74.2 additional anxiety-free days during the 12-month follow-up period compared with the usual care group. There were no differences in the mean number of primary care or mental health outpatient visits (although there were some differences in median numbers of visits). Costs for a variety of health services showed no differences between the groups except that the intervention group had significantly higher mean costs for psychiatric medications (US$589 versus US$486) and for total outpatient mental health services (US$862 versus US$722). Incremental cost-effectiveness per anxiety-free day (from a total mental health cost perspective) was US$3. Calculation of ratios from alternative cost perspectives led the authors to

conclude that the intervention may result in small cost savings, neutral costs, or an incremental cost of up to US$11 per anxiety-free day. As a large proportion of the additional costs in the intervention group were due to larger costs for SSRIs, the price of which may come down with the availability of generic fluoxetine hydrochloride, a sensitivity analyses was carried out on total mental health costs being based on half their current costs. This reduced the incremental cost-effective ratio to US$1.74 per anxiety-free day.

In a Spanish study, Salvador-Curulla (1995) assessed the health care costs for a group of 61 patients with panic disorder in the year prior to the commencement of (unspecified) treatment and the year following. Mean direct health care costs increased from $478 to $758 (59%) but overall there was a reduction in costs of 94% due to the substantial impact on working days lost. The patients showed significant improvements on a range of clinical outcomes, with 41 having complete remissions or minimal symptoms. This suggests that treatment was cost-effective to society. However, lost employment was costed using the human capital approach and this may have led to an exaggerated cost-offset effect.

6.2 Obsessive-compulsive disorder (OCD)

The US Epidemiologic Catchment Area study suggested an overall population lifetime prevalence for OCD of 2.5% (Karno et al. 1988) making it the fourth most common psychiatric disorder following the phobias, substance abuse and major depression. Studies carried out in Canada, Europe, Taiwan and Africa have revealed similar prevalence rates (Rasmussen & Eisen 1994). OCD commonly coexists with a number of Axis I disorders including panic disorder, social phobia, eating disorders and Tourette's disorder. A lifetime history of major depression has been reported in two-thirds of OCD patients, and 60% of OCD patients experience panic attacks.

Some of the economic impacts of OCD on both sufferers and their families are not obvious or easy to quantify, and as it is a chronic condition, with relatively early manifestation, many of these disabling effects and their associated costs could persist for some years. OCD is no longer seen as a rare and untreatable disorder and there is evidence of the pervasiveness and persistence of its costs. SSRIs appear to be the pharmacotherapy of choice, behaviour therapy is frequently helpful and neurosurgery is a final option (Griest 1994; Griest & Jefferson 1998). However, the cost-effectiveness of treatments remains largely unevaluated. Although in-patient costs are modest for people with OCD - in other clinical areas where in-patient costs are higher, this has often been the prompt for economic evaluations - the increasing use of more expensive drugs and the use of sometimes quite intensive psychotherapies ought to be raising questions about the relative cost-effectiveness of different treatment approaches.

Furthermore, stigma associated with the illness leads to under-treatment, which in itself leads to long-term economic consequences. This is especially the case for those without a comorbid disorder, indicating that it may often be the comorbidity that is treated or the comorbidity that initiates referral. In the US it has been suggested that 28% of OCD sufferers receive inappropriate treatment (Hollander 1997), and that it takes ten years between onset of symptoms and seeking out professional help, an additional six years to gain a correct diagnosis and another year to get appropriate treatment (Hollander et al. 1996). During this long period, the costs of inappropriate treatment, the high indirect costs of the disorder and the costs to individuals and their families will continue to increase.

Most cost-effectiveness studies are based on data collected from trials. An alternative method is to routinely collect data on health care inputs and outcomes in the form of clinical audit. McKenzie (1995) provide such data on patients with OCD (plus a small number with phobic disorders) receiving inpatient care at a specialised unit in London. Specific interventions are not evaluated (although they could be), but the authors show that it is possible to link outcomes to time inputs (and therefore costs), and to make comparisons between therapists, diagnostic groups and years.

6.3 Somatic disorders

One particular condition that can have a substantial impact on health care costs, particularly in the general medical sector, and social costs (in the form of lost employment) is somatoform disorder. Hiller et al (2003) report the results of a German cost-consequences analysis of cognitive behavioural therapy plus comprehensive psychiatric care for this condition. This was a naturalistic study (rather than an RCT) and offers insight into how CBT might be incorporated into a routine setting. Costs and outcomes were measured for two years prior to the intervention and two years following it, which was felt to be appropriate given the episodic nature of the condition. Cognitive behavioural therapy was shown to result in improvements in outcome, reduced costs and reduced days lost from work over time when compared to a waiting-list comparison group.

6.4 Post-traumatic stress disorder (PTSD)

PTSD is a disorder that may occur following a particularly traumatic event, such as witnessing accidents or violent events, war or the death of a family member or close friend. In a US study it was found to affect between 1-2% of the population (Helzer et al. 1987). Symptoms may include intrusive re-experiencing of the trauma, avoidant behaviours, and a set of symptoms of increased physiological arousal. In addition, depression and anxiety can be comorbid conditions. The impact of PTSD is not only felt by those people who suffer the disorder, but often also by their families, their work organisation, and the wider society. Some of these impacts can be seen as 'economic', having effects associated with personal income, the ability to work, productive contributions to the national economy, or the utilisation of treatment and support services.

Very few cost-effectiveness evaluations have been carried out in the area of posttraumatic stress disorder. One study that has been completed included a comparison of the cost-effectiveness of three types of in-patient care for ex-service personnel in the United States (Fontana & Rosenheck 1997). The models of care were long-stay PTSD units, short-stay assessment and brief-treatment units, and general psychiatric units. Clinical outcomes were significantly better for patients treated in short-stay or general psychiatric units compared to the long-stay care. The costs of the initial hospitalisation were measured and these, unsurprisingly, were substantially greater for the long-stay units. Health care costs for the remainder of the year following admission were greatest for the patients initially treated in general hospital units but this was not enough to offset the cost differential of the initial treatment period. It was not clear from the study whether specialised brief treatment was to be preferred to general hospital treatment, but both appeared to be more cost-effective than specialised long-stay treatment.

6.5 General anxiety disorders

Psychological problems among patients admitted for physical conditions may well prolong stays in hospital. Levenson (1992) tested the hypothesis that offering a brief psychiatric assessment at the start of an in-patient stay would reduce hospital costs. Patients were randomly allocated to receive such an assessment (n=256) or to receive care as usual (n=253). In addition, a contemporaneous control group were recruited (n=232). Patients in the two control groups were not prohibited from receiving psychiatric assessments. Although the focus was on any cost differences, the authors also measured illness severity. This did not differ between the groups, and costs were actually higher for the intervention patients. The latter group had more severe problems at baseline, and controlling for this removed any significant cost differences. The hypothesis was though rejected, although it was not known whether a more prolonged intervention would have had an impact on costs.

7. EVIDENCE: EATING DISORDERS

Eating disorders have become increasingly recognised over recent years. The UK GP Research Register 1993 data suggest that at the primary care level the overall age- and gender-adjusted incidence of anorexia nervosa (AN) is 4.2 per 100,000 population, peaking at 34 per 100,000 for women aged between 10 and 19 years. For bulimia nervosa (BN), the figure is higher at 12.2 per 100,000 population, with the highest incidence at 57 per 100,000 for women aged 20-39 (Turnbull et al. 1996). But even in well-resourced health systems, relatively few people are receiving specialist care: according to a recent review paper, perhaps only a third of a patients with anorexia in the community are coming into mental health care and only about 6% of patients with BN (Hoek et al. 2003).

There are only two studies that look at the national costs of eating disorders. Streigel-Moore (2000) estimated that in 1995, average US inpatient and outpatient treatment costs for one year were $6045 per person for AN and $2962 for BN. AN costs were similar to those for schizophrenia ($4824) but significantly higher than treatment costs for OCD ($1930). The authors suggest that these figures for eating disorders are underestimates as they rely on diagnostic codes used for billing. Thus, for example, entry through accident and emergency departments for problems associated with severe dehydration would not be included in these costs even where the underlying cause was AN. Streigel-Moore et al also point to considerable under treatment; empirically validated psychotherapeutic treatment commonly consists of 20 sessions whereas women in this database received an average of 16 visits and men only nine.

More recently Krauth et al. (2002) reported a fuller cost-of-illness study for Germany. Costs include hospitalisation, rehabilitation services, inability to work and premature death. Total direct costs were 65m Euros for AN and 10m Euros for BN. Compared to the US data, the inpatient costs for BN were about the same but much lower for AN, in part due to differences in the coverage of health care benefits in the two countries. The annual cost per AN patient was 5,300 Euros, 37 per cent of which is the direct costs of treatment. The cost per BN patient was 1,300 Euros of which direct treatment costs account for 12%. The authors note that these figures are likely to be underestimates as they exclude outpatient medical care (such as psychotherapy), pharmaceuticals and the loss of production due to incapacity to earn a living.

A review of the eating disorders literature aimed to synthesise information from efficacy studies to provide guidance for clinical practice and service provision (Treasure & Schmidt 1999). The authors looked at the evidence on service acceptability, matching services to severity, and the evidence around low and high intensity care models. The authors also noted that while there is some evidence on the

cost-effectiveness of BN services, there have been no economic evaluations of services for people with AN, or the more common eating disorders not otherwise specified (EDNOS).

7.1 Bulimia nervosa

Bulimia nervosa was only recognised as a distinct diagnostic category in 1979. Over the next fifteen years, several reviewers reported good outcomes from psychological therapies for people with BN (see for example, Mitchell et al. 1993). Olmsted (1991), for example, assessed the impact of a brief psycho-educational group intervention (ED) relative to individual cognitive behaviour therapy (CBT). The study had no formal cost component but the authors estimated the percent reduction in symptoms per therapist hour. This measure of the relationship between inputs (albeit a very narrow measure) and outcomes showed a 25% reduction in vomiting and objective bingeing per therapist hour for the ED group (n=25 completing treatment) and only a 5% reduction in these symptoms for the CBT group (n=29 completing treatment). However, CBT was generally more effective that ED and the most severely ill group did not respond to ED treatment.

Pharmacological treatments have also been identified as promising in the treatment of BN (Striegel-Moore et al. 2000). In one of the few studies to include an economic component, Koran et al undertook an exploratory post hoc study comparing five treatments for BN: 15 weeks of CBT followed by three monthly sessions; 16 weeks and 24 weeks of a tricyclic antidepressant medication; and CBT combined with medication for 24 and 16 weeks (Koran et al. 1995). Twenty-three patients received CBT only and 12 patients were in each of the other four treatment groups. Two outcome measures were selected: the proportion of patients who were abstinent from both binge-eating behaviours and purging at 32 weeks and one year from start of treatment; and the proportion of patients indulging in binge-eating or purging once a week or less over the same periods. The cost of completing the treatment plan was based on professional fees for sessions attended, medication and serum tests. No other costs were included. Comparisons of the median cost-per-successful-patient at 32 weeks showed non-significant differences between the most cost-effective treatment, medication for 16 weeks, and the least (medication and CBT for 16 weeks). One year after treatment began, medication for 24 weeks was the most effective and the least costly. However, evidence from other studies suggests that between 15 and 35% of BN patients treated with anti-depressants relapse over a 1-2 year period, but at 5-year follow-ups, patients treated with CBT have maintained their gains (Agras 2001).

Mitchell and colleagues (1999) also compared the costs of four treatments for BN for which the effectiveness studies had shown the percentage reduction in the frequencies of eating disorders and rates of abstinence to be comparable: individual CBT, two forms of Group CBT, and medication with serotonin reuptake inhibitors. A comparison of the mean cost (therapy only) per patient showed that the medication was less expensive than individual CBT but more expensive than either form of Group CBT.

Although slightly outside the remit of this review, two studies of obesity treatment were found that use a treatment cost per unit of weight approach to combining resource inputs and outcomes. Harvey-Berino (1998) found the treatment costs (only) of an interactive television approach to be less costly per pound of weight lost than standard therapist-led treatment ($2.00 v. $2.56). Agras (1990) found a computer programme without group support to be less costly per pound lost than the same programme with group support or a therapist-led weight loss programme.

7.2 Anorexia nervosa

There are no cost-effectiveness evaluations of services for people with AN, although we are aware of studies currently underway (there are, for instance, three studies currently underway at CEMH, Institute of Psychiatry in London). Findings from these studies will be come available over the next few years. Mitchell et al point out that anorexia nervosa is particularly hard to study due to its low prevalence, the need for multiple treatment cells, the associated medical risks, the difficulties of gaining informed consent from adolescents, and their poor treatment compliance (Mitchell et al. 1999). What can we glean in terms of information about costs and effectiveness from the literature?

- Treasure and Schmidt (1999 p.165) note that only broad indicators are currently available: '… specialist [AN] services, while perhaps more expensive, lead to better short-term outcomes … and have lower mortality rates…, thereby intimately reducing cost to the individual, their family and society.'

- Costs for AN should be considered wide-ranging. AN has a high mortality rate of around 0.6% per year, the highest of any functional disorder. Approximately half of the deaths results from medical complications and the remainder are suicides. Palmer and Treasure (1999 p.307) continue '…neither physical nor psychological effects can be neglected if services are to be optimal or safe.' Moreover, there are likely to be considerable out-of-pocket and lost production costs to the family and there may be supports used that are provided from non-health agencies.

- In a commentary on a review of a comparative effectiveness of inpatient and outpatient AN services, Crisp (1992) note that 'It was also striking that … the much less costly and relatively brief outpatient option did so well.' However, the authors were considering only the hospital-based costs of treatment. If full costs are considered the savings to society may be lower.

- There is some evidence that discharging patients with AN before they attain weight within the normal range might be a case of short-term saving and longer-term costs; people who are discharged early are more likely to be re-admitted as their eating behaviour is less likely to have changed. They have poorer clinical outcomes and a greater likelihood of becoming 'revolving door' patients (Baran et al. 1995).

- A small study in Leicester, England looked at the impact of opening of an intensive day programme for treatment of local patients with AN (Birchall et al. 2002). The number of bed-days for 12 patients in the three years prior to the day programme opening was compared to the number three years after (10 ward admissions, 5 day programme patients) and costs were calculated. The costs of the day programme were added to the latter total. (No other costs were considered.) Inpatient bed-days and overall costs had reduced since the day programme opened and 'the early results in terms of weight gain and readmission rates are promising' (p.336).

- Unlike BN treatments there is no clear evidence for the effectiveness of psychological therapies in AN as studies are often small and unrepresentative (Connan & Treasure 2000). Some evidence is emerging to suggest effectiveness of certain types of family therapy (Wilson 2003) and for year-long outpatient focal

psychodynamic psychotherapy and a 14-week course of family therapy over cognitive-analytic therapy or low contact routine treatment (Dare et al. 2001).

7.3 Service models

In one of the few studies to include patients with AN and BN, Williamson and Thaw (2001) explore the extent to which systematic application of admission guidelines and changes in the level of care can be used to reduce the costs of treating eating disorders. Using a decision-tree algorithm to assign patients to a particular level of care, subsequent movement (attending inpatient, day hospital, intensive outpatient, or outpatient facilities) was dependent on clinical progress. The same therapies (drugs, individual, family, support group) were available to all patients attending this regional medical centre. Outcomes (changes in body mass index and eating disorder symptoms) were equivalent for patients whose treatment had begun at the partial day hospital programme or as an inpatient, but hospital costs were lower for the day programme. Again the sample sizes are small: 36 patients with AN were included and 15 with BN; 28 were initially referred for inpatient treatment and 23 for partial day hospital treatment. As the authors point out, this study should not be seen as yielding a definitive answer of relative efficacy – or efficiency – of inpatient versus day hospital treatment. Moreover, the narrow cost measure disguises potentially high patient costs for the day programme (regardless of other costs); the authors' low estimate of the hotel costs borne by patients while attending the day programme absorbed 26% of the 'savings' over inpatient-initiated treatment.

7.4 Conclusions

The data on cost-effectiveness of BN services are sparse, and entirely absent for AN services. Although constituting the beginnings of a body of evidence on BN services, the studies that are reported above fall prey many of the common failings of economic evaluations; in particular the small sample sizes mean the relative cost-effectiveness findings are unlikely to be reliable. Commonly, only a narrow measure of costs has been employed, focussing on specialist treatment, usually in hospital environments. Evidence is emerging that eating disorders may have wider resource implications for other non-specialist and non-health services and well as families (Crow & Peterson 2003).

Many of the papers that are cited here use data from the early 1990s so are relatively old. In common with recent reviews, our focused systematic search of the databases did not reveal any more recent economic evaluations and only two cost-of-illness studies. Changing service systems in the US mean that new studies are warranted and, as the findings of service evaluations are not always transferable between countries, evaluations of eating disorder treatments and services in non-US countries are certainly required.

8. EVIDENCE: MENTAL HEALTH PROBLEMS IN OLD AGE

Our review of the published economic literature on interventions for mental health problems among older persons has generated only rather sparse findings. This is unfortunate in absolute terms given the ageing of populations around the world, and also unfortunate in relative terms given the quantity of economic evidence that now exists for persons below the age of 65. The available evidence is also not evenly spread: all of the economic evaluative studies of older people with mental health problems have focused on dementia. From a clinical viewpoint, this is not surprising, since while older people do suffer from most classifiable mental illnesses, they have a

much higher prevalence of dementia including Alzheimer's disease (AD). However what was unexpected was the finding that co-morbid neuro-behavioural economic aspects of dementia such as depression, emotional instability, apathy, irritability, and depressive diagnoses on their own have not received attention. Authors have argued that older adults with major depression are two to three times more likely to develop AD or some other irreversible dementia. While other studies have indicated that the symptoms of AD are likely to lead to depression, the causal relationship remains unclear.

Not only are there few economic evaluations of treatments for older people with mental health problems, but also older people are generally excluded from adult studies.

In the absence of evidence for other mental health problems, this section will focus on the economic evaluation evidence for older persons with dementia.

8.1 Pharmacological interventions

Drug interventions for dementia have been used to manage memory disturbance, behavioural disturbance and for disease modification. The most successful pharmacological approach in treating cognition is directed towards the loss of cholinergic function. This approach seeks to inhibit cholinesterase, and in turn raise the level of acetylcholine, potentially facilitating cholinergic transmission. The first available cholinesterase inhibitor approved by the FDA in 1986 was tacrine. Other drugs include donepezil, rivastigmine, and more recently galantamine were approved for the symptomatic treatment of patients with mild to moderate AD. A review of the clinical evidence suggests that in addition to improving cognitive ability, cholinesterase inhibitors appear to relieve behaviour symptoms and improve daily functioning (Clegg et al. 2001; Erkinjuntti et al. 2002; Rogers et al. 1998). However, relative efficacy across other domains remains unclear.

A recent review by Jönsson and colleagues (2002) of the cost-effectiveness of pharmacotherapy for individuals with dementia revealed a dearth of evidence. In assessing the evidence on the cost-effectiveness of tacrine, the authors conclude that poor tolerability of the drug makes it difficult for many patients to reach the dosage required to determine a clinically significant effect. Hence the cost-effectiveness of tacrine is doubtful. In the same review, the economic evidence of donepezil revealed five Markov modelling studies. A broad perspective was adopted in four of the studies, while the fifth included direct medical costs only. Donepezil was the dominant strategy in most of the studies, while in the other two studies donepezil treatment was more costly. Jönsson and colleagues conclude in favour of donepezil as a cost-effective option, with the caveat that it must be prescribed to the right patients at the right time. This is due to the finding that once the disease has passed the moderate level, further treatment may be of no benefit to the patient.

In our own updated review, two additional studies were located (Ikeda et al. 2002; Wimo et al. 2003). Wimo and colleagues evaluated the costs and consequences of donepezil and placebo in the treatment of patients with mild or moderate dementia in five Northern European countries. Measures of effectiveness were based on the Gottfries-Brane-Steen (GBS) scale, the Mini-Mental Status Examination (MMSE) the Global Deterioration Scale (GDS) and the Progressive Deterioration scale (PDS). Costs were measured from a societal perspective and the impact of treatment on the caregiver and the indirect cost of care determined using the Resources Utilisation in Dementia (RUD) questionnaire. The findings suggest that the overall cost was lower

for the donepezil group compared to the placebo treated group over the 52-week study period. However this difference was not significant. On the clinical measures of efficacy, significant differences were found in favour of donepezil over placebo on the GBS and the MMSE at 24, 36 and 52 weeks. When analyses of patients in decline for individual items on the Instrumental Activities of Daily Living (IADL) scale were analysed, the results suggest that fewer patients in the donepezil group deteriorated in individual IADL items at 52 weeks compared with placebo patients. The authors conclude in support of earlier findings (Jönsson et al. 1999; Neuman et al. 1999; O'Brien et al. 1999) that donepezil may prove a cost-effective alternative to no treatment.

Ikeda (2002) conclude that donepezil was dominant across sub-groups of diagnostic categories of AD in terms of low cost and high health outcomes. However the results should be treated with caution given the methodological limitations of this study.

Rivastigmine, another acetylcholinesterase inhibitor, has been found to be significantly beneficial in improving cognition. In addition to the study identified in the review conducted by Jönsson and colleagues (2002), Clegg et al. (2001) in their own review identified modelling studies by Hauber (2000a; 2000b). Though the evidence base is wider, Clegg suggests that the findings are harder to interpret due to exclusion of the effectiveness results and uncertainty surrounding the calculation of the cost-effectiveness ratios.

Previous reviews of the cost-effectiveness of galantamine have not revealed any studies. Our review found only one additional study. With such a narrow base the cost-effectiveness of galantamine is still in the balance. In this study Migliaccio-Walle (2003) evaluate the economic impact of galantamine 16 and 24 mg dosages relative to no pharmacological treatment in the management of mild and moderate AD in the US. The analysis was conducted using an AD predicted equation developed by members of the Assessment of Health Economics in AD study group (AHEAD). It was estimated that patients receiving galantamine were treated for a mean 32.8 months. The mean time in full time care was estimated to reduce to 19.9 months for patients on 16-mg and 19.4 months with the 24-mg dose. Cost included all paid formal care costs such as nursing home, inpatient care, physician visits, nursing care, emergency department visits and the costs of galantamine, but not those borne by patients and families. The authors' findings suggest that, despite the added cost of galantamine, a cost saving would accrue when compared with no treatment. Migliaccio-Walle and colleagues have conducted a costing study, though the authors have indicated that the results of efficacy from other studies may make galantamine treatment dominant over no treatment.

8.2 Non-pharmacological interventions

AD is the most common cause of dementia, followed by multi-infarct dementia. Given that no cure exists for AD, the primary goal of treatment has been to improve or enhance cognitive function (Lewko et al. 2002). Because the progression to AD occurs more frequently in patients with mild cognitive impairment than in the general elderly population, one of the challenges has been to identify which patients with mild cognitive impairment will develop AD. Imaging tools such as computed tomography (CT), single photon emission computed tomography (SPECT), magnetic resonance imaging (MRI) and dynamic susceptibility-weight contrast material-enhanced magnetic resonance imaging have been designed to predict which patients with mild cognitive impairment will progress to AD.

McMahon et al (2003) conducted the only economic study identified in our review that evaluated diagnostic tools. They focused on people living in community settings. They compared costs and quality-adjusted life years (QALYs) associated with three strategies involving single photon emission computed tomography (SPECT), dynamic susceptibility-weight contrast material-enhanced magnetic resonance (MR) imaging and positron emission tomography (PET) as functional imaging adjunct to the standard clinical work-up. Costs were specific to each of the strategies and included the cost of the standard examination. The cost of PET was based on resource use. The cost of data manipulation was added to the costs of Medicare reimbursements for visual SPEC, and since dynamic susceptibility-weight contrast material-enhanced magnetic resonance (MR) imaging was a new procedure its cost was estimated as being equal to Medicare reimbursements for MR imaging plus the cost of three-dimensional reconstruction of the image data. The results suggest that dynamic susceptibility-weight contrast material-enhanced magnetic resonance (MR) imaging may be preferable to PET for the diagnosis of AD. This result was shown to remain stable across scenarios in which drug treatment effectiveness and versions of the Health Utilities Index (for QALY measurement) were varied. The cost-effectiveness analysis of dynamic susceptibility-weight contrast material-enhanced magnetic resonance (MR) imaging was found to have a high cost per QALY compared to other strategies. The assumptions of the analysis are clearly stated. The authors conclude against the use of PET as a diagnostic tool in favour of other tools since by adding PET to the standard diagnostic regimen would yield limited benefits at a much higher cost. The benefits of such tools would be reassuring to older adults with mild memory complaints, and act as confirmation that their forgetfulness reflects a normal age-related change and probably will not progress. However, more evidence is needed to substantiate this result.

8.3 Conclusions

There are clearly many unanswered economic questions. Many of the economic evaluations identified from the review have centred on Alzheimer's disease. The weight of the evidence in large measure has been on cholinesterase inhibitors used in managing memory disturbance and with the potential to delay the need for institutional or full-time care. Of the cholinesterase inhibitors, tacrine and donepezil have been more widely explored for cost-effectiveness evidence. There has been very little work by economic evaluators on the treatment of depression among older people. There are further gaps in our knowledge about the appropriateness of non-pharmacological psychosocial interventions for individuals for whom tolerability to side-effects or adherence are issues, the use of interventions for preventing or delaying dementia, and community-based living versus independent living.

9. CONCLUSIONS

Growing awareness of the need to improve not only the effectiveness but also the cost-effectiveness of health care interventions has produced various streams of demand for economic evidence. There are requests for measures of the overall resource or cost impact of a particular health problem, leading to cost-of-illness and 'global burden' studies. A lot of attention has recently focused on some of the non-health care costs – which can be very large in mental health contexts. While cost-of-illness calculations can be helpful in order to raise awareness of the scale and breadth of impact of mental health problems, they are no substitute for evaluations that look at both costs and outcomes. There are also demands for economic evaluations of particular treatments or policies, generating cost-effectiveness and similar analyses, either carried out within clinical trials or using routinely collected, naturalistic data.

Third, there are searches for new service and health system reconfigurations that can improve the efficiency of use of available resources. Examples of such changes with potential efficiency consequences are the managed care changes in the US and the less dramatic developments in 'sectorisation', privatisation of provision and care programming in some European countries.

Well-conducted economic evaluations can therefore make important contributions to the discussion and development of policy and practice in the mental health field. They can support decisions relating to the funding and provision of services and can help to improve the efficiency with which scarce mental health and related resources are allocated.

In this paper we have reviewed the economic evaluation evidence in the mental health field, drawing on some new systematic searches of the international literature, as well as our own previous reviews in some diagnostic fields. We do not claim that the evidence is absolutely comprehensive, because there have undoubtedly been studies completed that have not been published in places that are easily found through electronic searches. Nevertheless, our searches have been conducted through a great many databases, including many that are not English language. We would therefore be disappointed and surprised if we had missed large numbers of important studies. We would, of course, be very interested to hear about other studies that have been carried out

What is clear from this review is that some fields are quite well served by economic evidence, whereas others have very little evidence of any quality to support or inform system-level or treatment-level decision-making. For example, the diagnostic fields of eating disorders, anxiety disorders, mental health problems in old age (with the exception of dementia) and child and adolescent mental health problems are fields where there are very few economics studies, and many of those that have been conducted are insufficiently robust to allow conclusions to be drawn.

What accounts for this huge variability in coverage and quality? A major influence on the prevalence of economic evaluation evidence is the development of new health technologies. In particular, the introduction of new drug classes is now almost always accompanied by a swathe of clinical and economic evidence. The evidence may not always be of as high a quality as one would wish; in particular it usually begins with simulation modelling studies, some of which are not always especially impressive. In fields where there has not been a major change in treatment modality, and also in fields that have been comparatively neglected by clinical researchers, it is perhaps not therefore surprising that there should be little economic evaluation evidence.

The quality of many studies is disappointing. Among the methodological weaknesses are:

- small sample sizes, leaving studies under-powered to test the economic hypothesis;
- the narrow measurement of costs;
- the relative rarity of randomised controlled trials, and hence few studies with strong internal validity;
- the comparative rarity, too, of large observational studies with appropriate standardisation, and hence limitations on the external validity of some evidence; and
- the rarity of cost-utility analyses and cost-benefit analyses, making it impossible to use the existing evidence base to make comparisons of resource efficiency outside the mental health system.

However, the quality does appear to be improving. A review of literature published very recently found that there were more cost-utility studies now being carried out in the mental health field, that more economic evaluations where based on RCT designs, that the breadth of cost-measurement was expanding, that the number of studies was also increasing (Byford et al. 2003c).

Economic evaluations of treatments for mental health problems are inherently context bound. These evaluations describe the consequences of both the illness and its treatment for service systems and social relations, and these latter will vary from country to country, and often from region to region. Making generalisations across countries is therefore more hazardous than with, say, clinical evaluations. The almost complete absence of economic evidence on mental health interventions for almost every health system of the world is therefore a major concern. An ongoing review of mental health economic evaluations in low- and middle-income countries has found very few studies (Byford et al. 2003a).

What is clear is the pervasive global need for more and better economic evaluative evidence on mental health interventions, whether pharmacological, psychological, service-based or other. There is also a need for better access to this information, with informed assistance so that non-economists can extract from the evidence base the relevant information for their needs.

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